Health Risk Assessment and Management of Chlorpyrifos Exposure among Rice Farmers in Ghana

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ABSTRACT

Pesticides are commonly applied in the agricultural sector of Ghana by farmers. Owing to weaknesses in regulations and unsafe practices, applicators of pesticides in the country are vulnerable to excessive exposure and consequent health risks. However, there is no information on the levels of pesticide exposure and associated health risks among applicators in Ghana. In addition, the rice sector of Ghanaian agriculture has been growing in recent years, with significant use of pesticides among commercial growers. Therefore, the objectives of this study were to evaluate the patterns, determinants, magnitude and health risks of pesticide exposure among rice farmers in Ghana.

In order to achieve the objectives, a representative cross-section of small-scale farmers who grow rice with irrigation in the catchment area of Kpone Irrigation Scheme (KIS) were recruited for the study. The research was based on the four-step health risk assessment framework of the United States’ National Research Council, which is generally accepted by regulatory agencies and researchers. Thus, the research involved hazard identification, exposure assessment, dose-response assessment and risk characterization. The hazard identification study with the farmers (n = 214), which was carried out by questionnaire survey, showed that chlorpyrifos was the most widely used pesticide with usage prevalence of 83%. The study also showed that pesticides were applied under unsafe conditions and all applicators had experienced symptoms compatible with pesticide poisoning, as described by the WHO.
Evaluation of exposure to chlorpyrifos among the applicators during a typical spray event was carried out, based on two approaches. These were (1) whole-body dosimetry assessment of dermal exposure, using Tyvek coverall, hand gloves and socks to sample chlorpyrifos residues of applicators (n = 24); and (2) urinary trichloro-2-pyridinol (TCP) assessment of overall exposure from six urine samples (one sample collected prior to application and five samples collected over five days after application) from each applicator (n = 21). The dermal exposure study showed that the percentage Unit Exposure (UE) value calculated from Total Dermal Exposure (TDE) was 0.03% and 0.06% among the median-exposed and the 5% highly-exposed groups, respectively. The study also indicated that the hands (39% of TDE) and the lower anatomical (82% of TDE) regions of the applicators were the most contaminated and potential sources of dermal exposure.

The urinary TCP assessment indicated that the mean elimination half-life (t_{1/2}) of chlorpyrifos in the body of the applicators was 50 hours, which is higher than those (27 to 43 hours) previously reported. The median absorbed dose of chlorpyrifos estimated from urinary TCP due to chronic background exposure (LADD_{B}), chronic application exposure (LADD_{A}) and acute application exposure (ADD_{A}) were 0.2 µg/kg/day (mean ± S.D of 0.3 ± 0.4 µg/kg/day), 0.1 µg/kg/day (mean ± S.D of 0.3± 0.3 µg/kg/day) and 6 µg/kg/day (mean ± S.D of 19 ± 24 µg/kg/day). The absorbed daily dose of chlorpyrifos estimated from urinary TCP and whole-body dermal dosimetry methods produced similar exposure estimates, based on the means ± S.D (15±22 and 16±7 µg/kg/day, respectively), with applicators who participated in both evaluations. The levels of chlorpyrifos exposure from occupational application were positively influenced by the
quantity of chlorpyrifos formulation applied, spraying duration, the number of spray tanks applied and the height of the crops sprayed (p < 0.05).

To evaluate the dose-response of chlorpyrifos, exposure data from human epidemiological studies from the scientific literature were collated. The exposure data associated with adverse effects were expressed as Cumulative Probability Distributions (CPDs) to obtain the Toxicant Sensitivity Distributions (TSDs) of chlorpyrifos for chronic and acute adverse effects. A guideline value determined at the 5th percentile of the TSD for chronic and acute adverse effects was 0.5 and 2 µg/kg/day, respectively. These guideline values derived with the TSD method are directly applicable to humans without the need for safety factors. On the other hand, conventional guideline values established by regulatory institutions require the application of safety factors when the No Observable Adverse Effect Level (NOAEL) or Lowest Observable Adverse Effect Level (LOAEL) methods are used.

Except for the guideline values set by the WHO which gave HQ < 1, those of the USEPA, APVMA and the TSD threshold dose at the 5th percentile gave HQ > 1, suggesting adverse health effects would be observed among the applicators. The percentages of the applicators who were likely to suffer adverse effects due to chlorpyrifos exposure were quantified with the Overall Risk Probability (ORP) and the Monte Carlo Simulation (MCS) techniques. The ORP and the MCS techniques showed that between 1 to 3%, 2 to 4% and 5 to 8% of the applicators were likely to suffer chronic adverse effects due to chlorpyrifos exposure from background, occupational application and combined exposure from background and occupational application,
respectively. Such chronic health effects may include altered thyroid functions and reductions in estradiol levels, based on the TSD. Also, the ORP and MCS techniques showed that between 31 to 33% and 32 to 34% of the applicators were likely to suffer acute health effects due to exposure from occupational application and combined exposure from background as well as occupational application, respectively. Comparison of these values with the TSD suggests that the acute health effects likely to be suffered by the applicators can include depression of cholinesterase activity, sub-clinical neuropathy and memory problems, particularly with occupational exposure.

Recommendations proposed for adoption by government institutions to help reduce pesticide exposure and associated health effects among the applicators, include provision of training and technical services to enhance adoption of Integrated Pest Management (IPM), promoting use of less toxic pesticides, regular training of farmers and Agricultural Extension Officers (AEOs) on pesticide safety and regular monitoring of exposure among applicators. It is also recommended that farmers should avoid excessive pesticide use, reduce spray duration, reduce number of spray tanks, practice good hygiene and use adequate PPE, particularly for the hands and the lower anatomical regions of the body.
STATEMENT OF ORIGINALITY

This work has not previously been submitted for a degree or diploma in any university. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made in the thesis itself.

__________________________
Albert Atabila
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LIST OF ABBREVIATIONS AND ACRONYMS

2,4-D  2,4-Dichlorophenoxyacetic acid
AChE  Acetylcholinesterase
ADD  Absorbed Daily Dose
ADD\text{A}  Absorbed Daily Dose from occupational application exposure
ADD\text{D}  Absorbed Daily Dose from dermal exposure
ADD\text{DEM}  Absorbed Daily Dose estimates from dermal dosimetry method
ADD\text{T}  Absorbed Daily Dose from both background and occupational exposure
ADD\text{TCP}  Absorbed Daily Dose estimates from urinary TCP method
ADF  African Development Fund
ADI  Acceptable Daily Intake
AEOs  Agricultural Extension Officers
AHED  Agricultural Handlers Exposure Database
AI  Active Ingredient
APP  Acute Pesticide Poisoning
APVMA  Australian Pesticides and Veterinary Medicines Authority
AT  Averaging Time
ATSDR  Agency for Toxic Substances and Disease Registry
AUD  Australian Dollar
AUE  Absorbed Unit Exposure
AUE\text{DEM}  Absorbed Unit Exposure values from dermal dosimetry method
AUE\text{TCP}  Absorbed Unit Exposure values from urinary TCP method
BH  Body Height
BMD  Bench Mark Dose
BuChE  Butyrylcholinesterase
BW  Body Weight
CDC  Centre for Disease Control and Prevention
CDI  Chronic Daily Intake
CP\text{5}  5\textsuperscript{th} Percentile Cumulative Probability
CP\text{50}  50\textsuperscript{th} Percentile Cumulative Probability
PCB  Polychlorinated biphenyl
PEL  Permissible Exposure Limit
PFPD  Pulsed Flame Photometric Detector
PHED  Pesticide Handlers Exposure Database
PON1  Paraoxonase 1
PPE  Personal Protective Equipment
PRA  Probabilistic Risk Assessment
QHFSS  Queensland Health Forensics and Scientific Services
QSAR  Quantitative Structure–Activity Relationship
RfC  Reference Concentration
RfD  Reference Dose
SF  Slope Factor
SSD  Species Sensitivity Distributions
STEL  Short-Term Exposure Limit
TCP  3,5,6-Trichloro-2-pyridinol
TDE  Total Dermal Exposure
TDI  Tolerable Daily Intake
TLV  Threshold Limit Value
TOs  Technical Officers
TSD  Toxicant Sensitivity Distribution
TSD_{ACUTE}  Toxicant Sensitivity Distribution for acute adverse effects
TSD_{CHRONIC}  Toxicant Sensitivity Distribution chronic adverse effects
TSDs  Toxicant Sensitivity Distributions
TSH  Thyroid Stimulating Hormones
UE  Unit Exposure
UNEP  United Nations Environment Programme
USEPA  United States Environmental Protection Agency
WHO  World Health Organization
WP  Wettable Powder

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CHAPTER 1
GENERAL INTRODUCTION

1.1 Background

Pesticides are chemicals used to prevent, destroy or control agricultural, forestry and public health pests (FAO, 1991). Functionally, pesticides can be grouped according to their target organism as insecticides, fungicides, herbicides, rodenticides, molluscicides or nematicides. Alternatively, pesticides can be classified based on their chemical structures, as inorganic or organic pesticides. The organic pesticides are sub-divided into chlorohydrocarbons, organophosphates, pyrethroids, carbamates, phenoxyacetic acids and so on.

The use of pesticides in agriculture has been practiced for a considerable time dating back to classical Greece and Rome (Lidén, 2006). Some of the earliest pesticides used were lime, sulfur, nicotine, pyrethrum, kerosene, and rotenone. Most of these forms of pesticides, however, lack potency with a wide range of insects, require repeated use due to their lack of persistence and are difficult to produce and use (Connell, 2005). The introduction of dichloro-diphenyl-trichloroethane (DDT) in 1939 by the Swiss chemist, Paul Muller marks a major development in insect control. DDT gained popularity and was widely used because of its relative long persistence, affordability, effectiveness, and broad-spectrum potency to a wide range of insects (Delaplane, 1996; Connell, 2005). The use of DDT and related chlorohydrocarbon insecticides, continued until 1962 when the book, Silent Spring was published by Rachel Carson, raising many possible ecological problems that could be associated with its use. Subsequently, the use of
DDT and other chlorohydrocarbon pesticides was severely restricted and phased out in many countries to protect human health and the environment (Boyd et al., 2003; Connell, 2005).

The restriction and phasing out of chlorohydrocarbon pesticides led to the increased use of other forms of pesticides such as organophosphates, carbamates, and pyrethroids. These classes of pesticides break down in the environment more rapidly and do not bioaccumulate, unlike chlorohydrocarbons (Connell, 2005; Krieger, 2010). However, they exhibit a variety of other harmful effects on human health and the natural environment.

Pesticides play an important role in modern agriculture and have contributed to increased crop yields throughout the world, thus helping to alleviate hunger and providing access to an adequate food supply. It is estimated that about 70% of crops produced globally could be lost due to pest attack, if pesticides are not used (Oerke, 2005). Owing to their importance in agriculture, more than 3.3 billion kilograms of pesticides are applied to crops around the world every year. Globally, pesticide production and use is increasing and it is estimated that by 2050, the global pesticide production level would be more than three times higher than the level in 2000 (Sexton et al., 2007). The increase in pesticide usage is influenced by the increasing need to supply affordable, good quality food that is free from pests and diseases (Delaplane, 1996).
Despite their beneficial characteristics in agriculture and other applications, the increased use of pesticides has some negative implications for human health and the natural environment, particularly in developing countries. About 3 million poisonings and more than 250,000 deaths related to pesticides occur yearly across the world with majority of the poisonings and deaths occurring in developing countries (WHO, 2004; Konradsen, 2007). Organophosphate insecticides are responsible for most of the pesticide-related deaths because they are highly toxic and the most widely used (Yang and Deng, 2007).

1.2 Rationale of the Study

The agricultural sector is a major driver of the economy of Ghana. It contributes about 30% to the GDP of the country and employs 45% of the active population, which is about 60% of the rural labor force. It also accounts for about 75% of export earnings and contributes to meeting more than 90 percent of the food needs of the country (World Bank, 2006; IFPRI, 2012). The rice sub-sector in Ghana has been growing in recent years in response to various interventions implemented by the Government of Ghana to encourage local production to meet the high demand for the crop (MoFA, 2009; Angelucci et al., 2013; Ragasa et al., 2013). The total area of land used for rice production increased from about 250,000 to 480,000 hectares between the years 2007 and 2011 (Ragasa et al., 2013).

Use of pesticides has been a major part of recent rice production systems in Ghana (Ragasa et al., 2013; Anang and Amikuzuno, 2015). This is mainly because of
significant problems posed by weeds, insects and diseases throughout the production stages of the crop (Kranjac-Berisavljevic’ et al., 2003). For example, yield losses of up to 100% and 30% due to rice blast infection and stem borers attack, respectively, have been reported (Nutsugah et al., 2003; Youdeowei, 2004). Also, contributing to this trend is promotion and advertisement by the pesticide industry (Ragasa et al., 2013). The Environmental Protection Agency of Ghana (EPAG), which is the main institution responsible for regulating pesticides in the country, faces challenges in the performance of its duties. These include financial, logistical and human resources inadequacies. Therefore, the pesticide regulatory system of the country has been weak (Afreh-Nuamah and Akotsen-Mensah, 2015). Also, pesticide use practices among applicators have largely been unsafe (Ntow et al., 2006; Mattah et al., 2015).

Residue monitoring studies in Ghana have shown that various pesticides used by farmers are present in food crops and other environmental media, with chlorpyrifos being one of the most common of the pesticides (Darko and Akoto, 2008; Ntow et al., 2008; Bempah et al., 2012; Botwe et al., 2012; Essumang et al., 2013; EPAG, 2016; Fosu-Mensah et al., 2016). Chlorpyrifos was detected in 68% of aquatic sediments sampled from farming communities (Botwe et al., 2012). The widespread presence of these residues provides evidence suggesting that applicators may be exposed to significant levels of pesticides, possibly due to unsafe application practices. Nevertheless, there has not been any study evaluating the levels of pesticide exposure and consequent health risks among applicators in Ghana.
1.3 Aims and Objectives of the Study

The aim of this study was to evaluate pesticide exposure and health risks among farmers in a rice growing community in Ghana. The specific objectives were to:

1. Identify hazardous pesticides and practices associated with the use of pesticides among applicators;
2. Assess the levels of chlorpyrifos exposure among applicators;
3. Evaluate the patterns of dermal exposure to chlorpyrifos among applicators
4. Review the dose-response relationship of chlorpyrifos exposure and adverse effects;
5. Characterize the risks of adverse health effects due to chlorpyrifos exposure among applicators; and
6. Propose strategies for reducing pesticide exposure among applicators

1.4 Significance of the Study

With agriculture being a major sector of the economy of Ghana, sustainable use of pesticides in the sector is necessary to ensure the overall success of the long-term development goals of the country. This study provides information on the levels of pesticide exposure and health risks in Ghana, as well as the strategies for reducing exposure. Therefore, the study offers guidance to authorities in both the agricultural and public health sectors on policy formulation towards pesticide risk management in the country and other countries with similar pesticide use settings. In addition, the study contributes to knowledge on the application of probabilistic techniques in health risk assessment and management of chemical pollutants.
1.5 Structure of the Thesis

Chapter 1- General Introduction:

Chapter 1 introduces the thesis by presenting the background, rationale, aim, objectives and significance of the research carried out in the thesis.

Chapter 2 - Literature Review on Pesticide Usage in Ghana, Related Health Effects and Behaviour in the Environment:

Chapter 2 presents a review of relevant literature on background information about Ghana, the agricultural sector, usage, regulation and public health implications of pesticides in the country. The chapter also provides a review on organophosphate insecticides and the behaviour of pesticides in the environment.

Chapter 3 - Literature Review on Human Health Risk Assessment of Chemicals in Natural and Occupational Environments:

Chapter 3 offers a review of literature on human health risk assessment of chemicals in the natural and occupational environments by outlining the steps involved in the risk assessment process.

Chapter 4 – Methodology:

Chapter 4 stipulates the details of the methodology adopted for the research, including the conceptual framework, location and population characteristics of the research. Also provided in the chapter are the data collection procedures of the research, which
involved hazard identification study based on questionnaires, dermal exposure to chlorpyrifos study based on the whole-body dosimetry technique, overall exposure to chlorpyrifos study based on urinary 3,5,6-Trichloro-2-Pyridinol (TCP), chlorpyrifos dose-response study and health risk characterization study based on both conventional and probabilistic techniques.

Chapter 5 - Hazard Identification with Rice Farmers in Ghana:

Chapter 5 presents the results and discussion of the hazard identification study of the research. The chapter provides information on the socio-demographic characteristics of the farmers studied pest problems, pesticide use, pesticide exposure risk factors and self-reported acute pesticide poisoning symptoms among the farmers.

Chapter 6 - Exposure Assessment of Chlorpyrifos with Applicators on Rice Farms in Ghana:

Chapter 6 outlines the results and discussion of the dermal and overall exposure studies. The results and discussion of the dermal exposure study include information on the personal characteristics of the applicators, observed field factors during application, Total Dermal Exposure (TDE), Unit Exposure (UE), patterns of dermal exposure, factors associated with TDE, Absorbed Daily Dose (ADD_D) and Lifetime Average Daily Dose (LADD_D) of chlorpyrifos from dermal exposure. With the overall exposure study, the results and discussion include information on the personal characteristics of the applicators, observed field factors during application, urinary creatinine levels, urinary TCP levels, elimination half-life of chlorpyrifos, estimated Absorbed Daily
Dose (ADD$_A$) and Lifetime Average Daily Dose (LADD$_A$) of chlorpyrifos and factors associated with ADD$_A$ levels found with the applicators.

Chapter 7 - Chlorpyrifos Dose-Response and Toxicant Sensitivity Distribution (TSD) Assessment:

Chapter 7 presents the results and discussion of the dose-response study. The chapter reviews dose-response data from the scientific literature used in establishing conventional chlorpyrifos guideline values as well as those derived using probabilistic techniques. This chapter highlights the advantages and disadvantages of the two techniques of deriving guideline values.

Chapter 8 - Risk Characterization of Chlorpyrifos Exposure with Applicators on Rice Farms in Ghana:

Chapter 8 presents the results and discussion of the chlorpyrifos health risk characterization studies based on both the conventional and probabilistic techniques. The chapter provides the Cumulative Probability Distribution (CPD) plots the chlorpyrifos absorbed dose estimates of the applicators, from the dermal and the overall exposure studies. The chapter also outlines the level of health risk from chlorpyrifos exposure among the applicators, obtained with the Hazard Quotient (HQ) technique at the 50$^{th}$ and 95$^{th}$ Cumulative Probability (CP) of exposure. In addition, the chapter provides information on the overall proportion of health risk among the applicators, obtained using the Overall Risk Probability (ORP) and Monte-Carlo Simulation (MCS) techniques.
Chapter 9 - General Conclusions and Recommendations:

Chapter 9 ends the thesis with the conclusions of the research and recommendations for improving pesticide safety among applicators. The recommendations were proposed for consideration by the Government of Ghana, pesticide applicators and researchers with interest in pesticide safety.
2.1 The Republic of Ghana

The Republic of Ghana, formerly called the Gold Coast, is one of 16 nations of the sub-region of West Africa located within latitude 4° 44’N and 11°11’N and 3° 11’W and 1°11’ E. It shares a border with Cote d’Ivoire to the west, Burkina Faso to the north, and Togo to the east. Ghana is bounded to the south by the Gulf of Guinea (the northeastern part of the tropical Atlantic Ocean) with a coastline of about 539 kilometers (Figure 2.1). Stretching across the length of the country is the prominent Volta River basin that drains into the Gulf of Guinea. The basin includes the Volta Lake which was created artificially and considered one of the largest artificial lakes in the world (Oppong-Anane, 2006; IFAD, 2012).

Accra is the capital town and the largest city of Ghana. The country is divided into 10 administrative regions and 216 Districts. The regions are Greater Accra, Volta, Ashanti, Brong Ahafo, Central, Eastern, Western, Northern, Upper East, and Upper West regions. The country has a population of about 28 million with a population growth rate of about 3.7% per annum. About half (51%) of Ghanaians live in urban areas (GSS, 2012; GSS, 2016).
Ghana is the second largest economy in West Africa and the twelfth largest in Africa (ADB, 2012). The informal sector is the largest, providing employment to about 80% of the labour force in Ghana (Osei Boateng, 2011). Ghana attained middle-income status in 2011 in advance of its 2015 Millennium Development Goals. However, about 29% of the population still lives below the poverty line (IFAD, 2012). The three main sectors of the economy of Ghana are service, industry and agriculture, with Gross Domestic Product (GDP) contributions of 58%, 22%, and 20%, respectively (GSS, 2015).
Figure 2.1: A Map of Ghana

2.2 Agriculture in Ghana

2.2.1 General Characteristics of Ghana’s Agricultural Sector

The agriculture sector is a key driver of the economy of Ghana, employing about 42% of the labor force (MoFA, 2013). About 90% of farms in Ghana are small scale in size (less than 2 hectares). The farming system is predominantly traditional with hoe and cutlass being the main farming tools. Food crop farms are mostly intercropped, although mono cropping is practiced on large-scale commercial farms. Agriculture in Ghana largely relies on rainfall with only about 2% of the potential irrigation area developed as at 2002 (MoFA, 2011a, 2013).

The main sub-sectors of the agricultural sector in Ghana in terms of contribution to GDP, is shown in Figure 2.2 (MoFA, 2011a). The largest contributor to agricultural GDP is the crop sub-sector, representing 75%. A list of the main types of crops grown in Ghana is provided in Table 2.1. Common crops grown in all the ecological zones of Ghana include rice, maize and tomato.
Figure 2.2: Agricultural sub-sectors of Ghana (MoFA, 2011a)

Table 2.1: The Main Types of Crops Grown in the Ecological Zones of Ghana

<table>
<thead>
<tr>
<th>Ecological Zone</th>
<th>Cereals</th>
<th>Roots and Tubers</th>
<th>Vegetables</th>
<th>Legumes</th>
<th>Trees</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rain Forest</td>
<td>maize, rice</td>
<td>cassava, plantain, banana, cocoyam</td>
<td>pepper, garden plant, okra</td>
<td></td>
<td>citrus, cocoa, coconut, oil-palm, rubber</td>
</tr>
<tr>
<td>Semi-deciduous</td>
<td>maize, rice</td>
<td>cassava, plantain, banana, cocoyam</td>
<td>tomato, pepper, garden plant, okra</td>
<td>cowpea</td>
<td>citrus, cocoa, coconut, oil-palm, coffee</td>
</tr>
<tr>
<td>Transition</td>
<td>maize, rice, sorghum</td>
<td>cassava, plantain, banana, cocoyam, yam</td>
<td>tomato, pepper, garden eggs, okra, cowpea, groundnut</td>
<td></td>
<td>citrus, coffee</td>
</tr>
<tr>
<td>Guinea Savannah</td>
<td>maize, rice, sorghum, millet</td>
<td>yam</td>
<td>tomato, onion</td>
<td>cowpea, groundnut</td>
<td>sheanut</td>
</tr>
<tr>
<td>Sudan Savannah</td>
<td>maize, rice, sorghum, millet</td>
<td>yam, sweet potato</td>
<td>tomato, onion</td>
<td>cowpea, groundnut</td>
<td>sheanut</td>
</tr>
<tr>
<td>Coastal Savanna</td>
<td>maize, rice</td>
<td>cassava</td>
<td>tomato, shallot</td>
<td></td>
<td>coconut</td>
</tr>
</tbody>
</table>

(Gerken et al., 2001; MoFA, 2011a; MoFA, 2011b)
2.2.2 Rice Production

Rice is ranked second to maize as the most important staple food in Ghana. Per capita consumption of rice increased from 17.5 kg per annum in 1999 to 38 kg per annum in 2008. The per capita consumption is projected to reach 63 kg per annum by 2018 (MoFA, 2009). The productivity of rice crop in Ghana is estimated to be about 2.5 tons/ha compared to a potential of about 7 tons/ha. This situation is attributable to low adoption of improved production inputs and technologies (Angelucci et al., 2013; Ragasa et al., 2013). Thus, local rice production has not been able to meet high demand for the crop. About 60% of rice consumed in the country is imported from countries such as the USA, Thailand and Vietnam (Kranjac-Berisavljevic’ et al., 2003; Breisinger et al., 2012; Ragasa et al., 2013). Rice importation cost Ghana about US$ 140 million annually (MoFA, 2011a).

To reduce reliance on imported rice and the associated pressure on foreign-exchange reserves of the country, the Government of Ghana and its development partners have initiated policies and programs to encourage more local rice production. These include the National Rice Development Strategy (NRDS), National Fertilizer Subsidy Program, seed subsidy program and rice import levies. The NRDS was launched in 2009 with the aim of increasing local rice production by 10% annually, promoting consumption of local rice, creating demand for rice by-products and promoting dialogue among stakeholders to build efficient information sharing and linkages (MoFA, 2009; Angelucci et al., 2013; Ragasa et al., 2013). These interventions have contributed to growth in local rice production in the country in recent years, in terms of area cultivated (hectares), production (metric tons) and yield (tons/hectare/year) (Figure 2.3) (Ragasa et al., 2013).
Use of pesticides has been a major part of recent rice production systems in Ghana (Gerken et al., 2001; Ragasa et al., 2013; Anang and Amikuzuno, 2015). This is mainly because of significant problems posed by weeds, insects, diseases and fungus throughout the production stages of the crop (Kranjac-Berisavljevic’ et al., 2003). Also, contributing to this trend is the intense promotion and advertisement by the pesticide industry (Ragasa et al., 2013).

Figure 2.3: Area cultivated, production and yield of paddy rice in Ghana, 1993–2011 (Ragasa et al., 2013)
2.3 Pesticide Usage in Ghana

2.3.1 Background

Small scale subsistence farming is the major type of farming system in Ghana. With this system, growing crops to feed families is the main concern of farmers. Consequently, use of agricultural inputs is minimal. However, with expansion of the economy of the country, agricultural lands have been lost to urbanization and there is more demand for agricultural products. These situations have led to increase in commercial farming with consequent intensive use of agricultural inputs such as pesticides. Pesticides are mainly applied on crops such as cereals, cocoa, vegetables, legumes and cotton (Gerken et al., 2001).

The earliest forms of pesticides used in Ghana were chlorohydrocarbons such as DDT. This class of pesticides were most preferred for controlling pests in both the agricultural and public health sectors since the 1940s until 1985. The importation, manufacture and use of most chlorohydrocarbons (aldrin, chlordane, dieldrin, DDT, heptachlor, hexachlorobenzene, mirex, and toxaphene) were officially banned in 1985 due to their toxicity, persistence, and bio-accumulative tendencies. Lindane was however allowed for restricted use to control pests of cocoa but was subsequently banned in 2001 (Ntow, 2001; Hogarh et al., 2014). Following the ban of chlorohydrocarbons, new classes of pesticides such as organophosphates, pyrethroids, carbamates were introduced.

2.3.2 Quantities and Types of Pesticides Used in Ghana

The total quantity of pesticides imported into Ghana increased from 7,763 metric tonnes in the year 2002 to 27,886 metric tonnes in 2006, which represents an increment of
about 259% within a period of four years (Figure 2.4) (Fianko et al., 2011). It must be remembered however that official figures of pesticide imports do not reflect quantities imported into the country through unofficial and unapproved routes as well as pesticide donations from development partners (Gerken et al., 2001; Williamson, 2003). It is therefore possible that the figures shown above could underestimate the actual quantities.

Figure 2.4: Quantities of Pesticides Imported to Ghana (Fianko et al., 2011)

The main types of pesticides, based on functional groups, registered for use in Ghana is shown in Figure 2.5. As at 2005, a total of 508 types of pesticides had been registered. This includes herbicides (42%), insecticides (40%) and fungicides (13%). Studies
conducted to monitor pesticides residues in environmental and dietary media show that organophosphate class, particularly chlorpyrifos, is the most commonly used (Amoah et al., 2006; Darko and Akoto, 2008; Essumang et al., 2008; Ntow et al., 2008; Bempah et al., 2012; Botwe et al., 2012; Essumang et al., 2013; EPAG, 2016; Fosu-Mensah et al., 2016). The study conducted by Botwe et al. (2012) indicated that chlorpyrifos was detected in 68% of water sediments sampled from farming communities. Also, a study conducted among pineapple farmers showed that about 81% of them applied chlorpyrifos (Tordzagla et al., 2013). According to the pineapple farmers, they use chlorpyrifos often because it controls a broad range of insects on pineapples as well as other crops.

Figure 2.5: Groups of Pesticides Registered for Use in Ghana (EPAG, 2016).
2.4 Pesticide Regulation and Management in Ghana

2.4.1 Mandated Institutions

The Environmental Protection Agency of Ghana (EPAG) is the organization given the mandate to protect and improve the environment in Ghana. As part of its mandate, the EPAG is responsible for the regulation and management of chemicals, including pesticides. The EPAG is given support by the Pesticides Technical Committee for the regulation and management of pesticides in the country. This committee is composed of members drawn from the EPAG, Ministry of Food and Agriculture, Ghana Cocoa Board, Ministry of Health, Customs and Excise Preventive Service, Ghana Atomic Energy Commission, Ghana Standards Authority, Food and Drugs Authority, Association of Ghana Industries, Ministry of Environment Science and Technology and representatives of farmers and pesticide dealers’ association. The work of the committee is coordinated by the EPAG (Gerken et al., 2001; EPAG, 2016). The EPAG is represented in all the ten regions of Ghana. Through its Chemical Control and Management Centre, the agency issues a list of registered as well as banned pesticides to the public at regular intervals (MoFA, 2011b).

2.4.2 Legal Framework

The two main laws that regulate the pesticides industry in Ghana are the Pesticides Control and Management Act, 1996 (Act 528) and part two of the Environmental Protection Agency Act, 1994 (Act 490) (EPAG, 2007). These laws set the legal framework for the registration, manufacturing, use, disposal and non-disclosure of information, classification, licensing, reporting, labeling, advertisement and inspections.
of pesticides. Other laws include the Food and Drugs Law, 1992 (Provisional National Defense Council Law 305B). This law controls the manufacture, import, export, distribution, sale, use and advertisement of foods, drugs, cosmetics, household chemicals and medical devices. Another law that plays a role in the regulation of pesticides in the country is the Plants and Fertilizer Act 803 (2010) (MoFA, 2011b). The law gives mandate to the Pesticide and Fertilizer Regulatory Division of the Ministry of Food and Agriculture to supervise and train regulatory inspectors, publish information materials on pesticides and keep records of pesticides in the country. Moreover, the division registers and provides training to pesticides dealers and applicators.

Apart from national regulations, Ghana has ratified several international conventions aimed to help regulate pesticides in member countries. These include the International Code of Conduct for the Distribution and Use of Pesticides, The Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal, Rotterdam Convention on Prior Informed Consent (PIC) and Stockholm Convention on Persistent Organic Pollutants (POPs) (MoFA, 2016).

**2.4.3 Registration of Pesticides and Licensing of Dealers**

Acts 528 and 490 require that all pesticides be registered accordingly by the EPAG before the importation, export, manufacture, sale or use of pesticides in the country. However, exemptions are possible if the pesticide is for research, national emergency or in transit to another country. It may also be allowed for unregistered pesticide to be to
be produced and exported to another country provided the importing country’s requirements are fulfilled. Approval for registration and licensing is based on evaluation of scientific data on the pesticide under consideration. The pesticide should be found to be effective for the intended use. In addition, it should not be harmful to human health and the environment (EPAG, 2007; EPAG, 2016).

It is also required by the Acts for pesticide dealers, such as importers, retailers, distributors, pest controllers, formulators, and warehouse operators to obtain license before they can operate. Other requirements include proper labeling and packaging of products, supervision of pesticide application by authorized persons, use of appropriate personal protective equipment or clothing during the handling and use of pesticides, notifying users of the dangers of the pesticide, and responsible use of pesticides (EPAG, 2007).

The major challenges facing the EPAG in the performance of its duties include inadequate financial and human resources. Consequently, the EPAG is sometimes unable to fully evaluate pesticides before approving registration and licensing. Also, the agency is not in the position to adequately control and monitor the importation of unapproved pesticides into the country (Tripp, 2003; EPAG, 2007). These situations, may put users of pesticides and the general population as well as the environment in Ghana at risk of exposure.
2.4.4 Distribution and Marketing of Pesticides

Pesticides used in Ghana are imported by multinational and national companies. Notable among them are Wienco Ltd, Dizengoff Ltd, CHEMICO Ltd, Reiss & Co. Ltd, and Calli Ghana Ltd (Bump et al., 2002; MoFA, 2011b). Majority of these pesticides are however retailed by informal petty dealers who are mostly unlicensed (Williamson, 2003). This situation shows a weakness in the implementation of Acts 528 and 490 of the Environmental Protection Agency of Ghana. However, farmers who produce vegetables and fruits for export are required by their associations to buy pesticides from only approved dealers. This is to ensure that their products meet international market regulations. Such organized groups also benefit from training on safe use of pesticides and credit facilities to obtain pesticides.

The informal distribution and marketing of pesticides is confronted with challenges. For instance, to make pesticides products affordable, some private pesticide dealers re-package the products into smaller bags. Most of these re-packaged products do not usually have adequate labels that give instructions for their safe handling and use. Moreover, re-packaged products may enter Ghana from neighboring countries with product labels written in foreign languages that the Ghanaian farmer cannot read and/or understand (Bump et al., 2002; Williamson, 2003). Also, some of the pesticides sold in the informal sector are of suspicious quality and dealers have no or inadequate knowledge about the products being sold. Owing to poor regulation of the pesticide industry, significant quantities of obsolete and dangerous pesticides can be found on the Ghanaian market (Bump et al., 2002; Williamson, 2003; MoFA, 2011b). In addition, retail shops generally have poor storage and ventilation conditions and operators of the
shop do not use adequate PPEs, putting their own safety and health at considerable risk. Consequently, many of the shop operators complain of disease conditions such as skin rashes, headaches, and dizziness (Bump et al., 2002).

### 2.4.5 Pest Management Policy of Ghana

Conventional pest management mainly based on application of synthetic pesticides was the pest control policy of Ghana’s Ministry of Food Agriculture (MoFA) until the adoption of Integrated Pest Management (IPM) in 1992, in conformity to global trend (Afreh-Nuamah and Akotsen-Mensah, 2015; MoFA, 2016). IPM is the application of a combination of appropriate pest control strategies to maintain or improve productivity in a way that reduces pesticides use and their adverse effects on human health and the environment. The range of strategies may include biological, cultural and chemical practices. The approach encourages natural pest control mechanisms leading to minimal disruption to agro-ecological systems (Veres, 2013).

A study among Ghanaian cocoa farmers showed that adoption of IPM increased crop yield about 64% compared to conventional pest control approach (Dormon et al., 2007). Also, IPM has been found to contribute to reduced levels of pesticide exposure and health effects, such as birth defects and abortion among farmers and farming communities (Crisostomo and Molina, 2002; Jirachaiyabhas et al., 2004). Despite their beneficial characteristics, adoption rate of IPM in Ghana has been low. Major challenges impacting adoption include inadequate training, technical support and policies; difficulty in controlling pests with IPM compared to conventional pest
management strategies with the use of pesticides; and promotion of pesticides by the pesticides industry (Parsa et al., 2014).

2.5 Public Health Implications of Pesticides Exposure in Ghana

2.5.1 General Pesticide Health Problems in Developing Countries

It is estimated that about 3 million poisonings and 220,000 deaths related to pesticides occur yearly across the world. About 90% of the poisonings and 99% of the deaths occur in developing countries, although pesticide use in these countries account for only about 25% of the total quantity used worldwide (FAO/UNEP/WHO, 2004; Landrigan and Claudio, 2008). A conservative estimate of the cost of pesticide related diseases and harm in sub-Saharan Africa in 2005 was found to be about USD $4.4 billion. This cost is expected to increase to about US$ 90 billion by 2020 (UNEP, 2012). OPs are responsible for majority of the pesticide-related deaths because they are highly toxic (Yang and Deng, 2007). Compared to chlorohydrocarbons, OPs do not persist in the environment. However, their acute toxicity is generally higher than chlorohydrocarbons (Connell, 2005).

The high pesticide-related health burden in developing countries is mainly due to intense usage, unsafe practices, and weak regulation and education. Also, the public health systems of these nations have inadequate capacities to adequately deal with pesticide-related health problems. This situation is made worse by the many different types of pesticides in use, which require different case management protocols (Bertolote et al., 2006; Konradsen, 2007). In addition, highly toxic pesticides that have been
banned in developed countries continue to be used in many of these countries (Landrigan and Claudio, 2008).

2.5.2 Pesticide Exposure and Health Problems in Ghana

Weaknesses in the pesticide regulation system, in addition to low level of pesticide use knowledge in Ghana have led to unsafe handling practices among applicators. These include inadequate use of Personal Protective Equipment (PPE) (Ntow et al., 2006; Aen Ngibise et al., 2015; Afari-Sefa et al., 2015; Mattah et al., 2015; Okoffo et al., 2016), storage of pesticides in household premises (Mattah et al., 2015), mixing of different types of pesticides for application (Mattah et al., 2015), inappropriate disposal of empty pesticide containers (Ntow et al., 2006; Afari-Sefa et al., 2015; Mattah et al., 2015; Okoffo et al., 2016), mixing pesticides with bare hands (Okoffo et al., 2016), drinking water or eating while spraying (Okoffo et al., 2016) and re-entering sprayed areas after few hours (Afari-Sefa et al., 2015; Okoffo et al., 2016). These situations may expose applicators to excessive levels of pesticides.

Inhibition of the activity of cholinesterase, an enzyme required for proper functioning of the nervous system, has been recognized as an indicator of exposure to organophosphate and carbamate pesticides (Zhao et al., 2006; Lionetto et al., 2013; Strelitz et al., 2014). A study carried out in Ghana by Ntow et al. (2009) to assess possible health problems associated with the use of organophosphate pesticides among farmers showed that cholinesterase levels among vegetable farmers (mean, 3.6 lmol/min/ml blood) were significantly lower than the levels (7.3 lmol/min/ml blood) found with a control group.
(p < 0.001). Also, about 97% of the farmers had experienced symptoms such as body weakness, headache, stomach pain, vomiting and skin itching. The numbers of symptoms were significantly higher than those found with the control group (p < 0.05). These symptoms are compatible with acute pesticide poisoning symptoms as described by the Intergovernmental Forum on Chemical Safety (IFCS) of the WHO (Thundiyil, 2008). Moreover, Ae-Ngibise et al. (2015) have found among members of a farming community who applied pesticides either at farm or home that between 27% to 39% of them had experienced pesticide poisoning symptoms. The study also reported that most (69%) women interviewed were involved with pesticide application. Of these women, more than half (51%) carried babies at their back whiles applying pesticides. In addition, a study among pregnant women in a rural community in Ghana showed that about 90%, 76% and 71% had detectable levels of organophosphates, pyrethroids and 2,4-D urinary metabolites, respectively (Wylie et al., 2017). These findings show that, apart from applicators, spouses and children are vulnerable to pesticide exposure and consequent health risks.

2.6 Organophosphate Insecticides

2.6.1 General Characteristics

Organophosphates are a group of insecticides that are used to control agricultural, horticultural, forestry, and public health pests, amongst others. Organophosphates were previously not considered appropriate for agricultural use because they were toxic to mammals. However, chemicals of this class were developed for use in agriculture as an
alternative when chlorohydrocarbons were found to cause many environmental problems.

The general chemical structure of organophosphates is shown in Figure 2.6. The chemical structure of organophosphates consists of a central phosphorous atom with a double bond to a sulfur or oxygen, R1, and R2 groups (which may be an ethyl or methyl in structure), and a leaving group that is specific to the individual organophosphate (see Section 3.1.2) (Connell, 2005).

![Figure 2.6: General Chemical Structure of Organophosphates](image)

Mostly, the R group can either be a methyl or an ethyl. Also, in some compounds the oxygen in the OX group may be substituted by sulfur. Examples of organophosphate insecticides include chlorpyrifos, malathion, parathion, dichlorvos, and dimethoate. The nerve gases soman, sarin and tabun also belong to the organophosphate class. The chemical structures of some common organophosphate insecticides are shown in Figure 2.7.
2.6.2 Mechanism of Action of Organophosphate Pesticides

Organophosphate insecticides are designed to kill insects through interference of the nervous system. Similar mechanism operates with human beings. Upon exposure and absorption, organophosphates may undergo metabolic bioactivation through oxidative desulfuration that replaces the sulfur at the double bond of the central phosphorus with oxygen, leading to the formation of the oxo forms of the parent organophosphate. This process is mediated by cytochrome P450 enzymes mainly in the liver (Chambers et al., 2001b; Costa, 2006). Metabolism of chlorpyrifos is shown as an example in Figures 2.8 to 2.10.
Figure 2.8: Hepatic Metabolic Activation of Chlorpyrifos to Chlorpyrifos-Oxon

Figure 2.9: Metabolic Detoxification of Chlorpyrifos-Oxon

Figure 2.10: Hydrolysis of Chlorpyrifos to Diethylthiophosphate and 3, 5, 6-Trichloro-2-pyridinol (TCP).
The oxon form of organophosphate reacts with available cholinesterase in exposed persons via phosphorylation leading to cholinesterase inhibition (Costa, 2006; Eaton et al., 2008). Cholinesterases are a group of enzymes responsible for degrading the neurotransmitter, acetylcholine, allowing a cholinergic neuron to return to its resting state after being activated. The two main types of cholinesterase are acetylcholine-cholinesterase found in many types of conducting tissues and red blood cells; and butyrylcholinesterase (Pseudocholinesterase) - found mainly in the liver as well as in blood plasma (Čolović et al., 2013). The inhibition of acetylcholinesterase leads to the build-up of excess acetylcholine at their sites of action, which in turn result in the over-stimulation of the cholinergic nerve terminals (Costa, 2006; Yang and Deng, 2007). Ultimately, the normal functioning of the nervous systems can be hampered.

The oxon forms of organophosphates may be detoxified through catalytic hydrolysis by the enzyme paraoxonase 1(PON1) (Costa, 2006) (Figure 2.9). Some organophosphates may not undergo the desulfuration process but rather be hydrolyzed to form it specific metabolite or a non-specific OP metabolite-dialkyphosphate (DAP) (Figure 2.10), which are then excreted in the urine. For instance, chlorpyrifos may be metabolized to its specific metabolite 3, 4, 6-trichloro-2-pyridinol (TCP) (Nolan et al., 1984).

### 2.6.3 Acute Health Effects

Acute toxicity of OPs usually begins to develop within few minutes to several hours after poisoning. The principal acute health effect of OPs is inhibition of acetylcholinesterase in both the Central Nervous System and the Peripheral Nervous
System and subsequent over-stimulation of nerve terminals in the nervous system. Over-stimulation of nerve terminals in the central nervous system may produce symptoms such as confusion, hypothermia, tremors, paralysis and coma, whilst over-stimulation in the peripheral nervous system may be characterized by bradycardia, hypotension, miosis, gastrointestinal distress and lacrimation tachycardia, fasciculation, ataxia, convulsions, and paralysis (Costa, 2006; Yang and Deng, 2007). Usually, symptoms of acute poisoning begin to occur when there is 50% or more inhibition of acetylcholinesterase. At 90% or more inhibition, death may result (Maroni et al., 2000). Death due to OP poisoning is mainly due to failure of the respiratory system following bronchoconstriction, increase in bronchial secretions, paralysis of the intercostal and diaphragmatic muscle, and inhibition of respiratory centers in the brain stem (Yang and Deng, 2007).

Severe acute OP poisoning may be treated by administering medications such as pralidoxime iodide, diazepam, atropine sulfate and glycopyrrolate to neutralize the effect of excessive levels of acetylcholine in the nervous system (Chambers et al., 2001a).

2.6.4 Chronic Health Effects

Chronic health effects from OPs may be due to secondary effects following the occurrence of an acute poisoning. One of such effects is Intermediate Syndrome (IMS), which was first described in Sri Lanka in 1987, with patients who had ingested OP pesticide in a suicide attempt. The syndrome was so described because it occurs in between the end of acute cholinergic crisis and the beginning of organophosphate-
induced delayed neuropathy (OPIDN) (Senanayake and Karalliedde, 1987; Costa, 2008). The signs and symptoms of IMS include weakness of proximal limb muscles, neck muscles, respiratory muscles, and motor cranial nerves (Senanayake and Karalliedde, 1987). Intermediate Syndrome is associated with many of the morbidity and mortality of OP poisoning; however, its underlying mechanism of pathophysiology is not well understood (Yang and Deng, 2007).

Another chronic effect following acute OP poisoning is organophosphate-induced delayed neuropathy (OPIDN), which occurs when certain OPs inhibit the enzyme, “neuropathy target esterase” (NTE) leading to damage to the afferent fibers of the central and peripheral nervous systems. The main signs and symptom of OPIDN may include, weakness, paralysis, tingling in the lower and upper extremities (Lotti and Moretto, 2005). The symptoms of OPIDN may start from 2-3 weeks after an acute exposure, when cholinergic and intermediate syndrome has lessened (Kozawa et al., 2009). The signs and symptoms of OPIDN are exhibited when there is phosphorylation and ‘aging’ of about 70% or more of NTE (Costa, 2006).

### 2.6.5 Chlorpyrifos

Chlorpyrifos [O, O-diethyl O-(3, 5, 6-trichloro-2-pyridyl) phosphorothioate] is a crystalline broad-spectrum organophosphate insecticide that is registered in more than 98 countries to control pests of over 50 crops. Dow AgroSciences is the primary producer of chlorpyrifos and it was first registered in the United States in 1965 (Martinez et al., 2004; Gomez, 2009). It comes under various trade names such as
dursban, lordsban, cobalt, nufos, warhawk and hatchet. It is sold in many different commercial formulation types including emulsifiable concentrate (EC), wettable powder (WP), granular (G) and micro-encapsulated emulsion (ME) (Gomez, 2009).

Chlorpyrifos has a vapour pressure of $1.0 \times 10^{-3}$ Pa at 25°C, water solubility of 0.4 mg/L at 19.5°C and an octanol/water partition coefficient (log $K_{OW}$) of 5.0 at 25°C (WHO, 2009c). It therefore exhibits some volatile properties and tend to partition from aqueous to organic phases in the environment. The insecticide is non-persistent in human body with an elimination half-life of about 27 to 43 hours (Nolan et al., 1984; Griffin et al., 1999; Williams et al., 2004; Meuling et al., 2005; Wang et al., 2016). Its main degradation product, TCP, is primarily eliminated through urine.

Chlorpyrifos is moderately toxic (WHO toxicity Class II) to human beings upon exposure (WHO, 2010). As an organophosphate, its main mechanism of toxicity is through inhibition of acetylcholinesterase in the nervous system, leading to over-stimulation of acetylcholine receptors and neurotoxicity (Costa, 2006). Chlorpyrifos is known to cause acute health effects such as depression of cholinesterase activity, sub-clinical neuropathy and memory problems, particularly with occupational exposure (Steenland et al., 2000; Albers et al., 2007; Farahat et al., 2011). The insecticide is not carcinogenic, however, other chronic health effects such as fetal neurodevelopment defects, altered thyroid functions and reductions in estradiol levels, may result from exposure (Berkowitz et al., 2004; Meeker et al., 2006; Meeker et al., 2008).
2.7 Behavior of Chlorpyrifos in the Environment

2.7.1 Background

The behavior of most pesticides, including chlorpyrifos, are governed by the same environmental processes. When pesticides are applied, they may undergo many physical (e.g. drift, run-off, and volatilization), chemical (e.g. hydrolysis, oxidation,) or biological (e.g. microbial degradation) processes (Kookana et al., 2002). Some key environmental processes affecting the fate of pesticides are illustrated in Figure 2.11. The environment consists of different phases such as the atmosphere, water, soil, sediment, suspended sediment and biota. Each of these phase is physically distinct, relatively homogenous within which pesticides behave uniformly (Connell, 2005). Based upon their physicochemical properties, pesticides released into the environment will partition amongst the various phases (Kookana et al., 2002; Connell, 2005; Gavrilescu, 2005). The most prominent of the physicochemical properties governing the fate of chemicals are vapor pressure, solubility in water and octanol-water partition coefficient. These properties will in turn be reflected in environmental processes such as volatilization, sorption-desorption, leaching and degradation. The properties of chemicals and processes they can undergo influence their potential to cause public health and environmental adverse effects.
2.7.2 Degradation and Transformation of Pesticides

Microbial Degradation and Transformation

Soil microorganisms such as fungi, bacteria, actinomycetes and algae may transform pesticides in three main ways - biodegradation, co-metabolism and bioaccumulation. Because all of these organisms obey the standard growth curve, there will always be an initial lag phase in any observed biological process. In contrast, non-biological decomposition starts immediately the pesticide reaches the soil during co-metabolism. There may also be a certain level of degradation as a result of the action of non-specific extracellular enzymes (e.g. esterases and hydrolases) that happen to be present in the soil. During this process, the pesticide is transformed but does not serve as a direct
source of energy to the microbes. In the case of accumulation, the pesticides enter the soil microbes through active and passive processes and accumulate in the organisms (Müller et al., 2007).

Factors affecting microbial degradation of pesticides in soil include organic matter content, moisture, temperature, aeration, and pH. The rate of microbial degradation increases when the soil is rich with organic matter, warm and moist with a neutral pH. Microbial degradation also depends on the ability of the microorganisms to produce the necessary enzymes to attack the pesticide (Connell, 2005; Gavrilescu, 2005). Generally, microbial degradation occurs mostly in the root zones of soils and much less in deeper soils, sediments and ground water. In heavy soils, biodegradation is particularly restricted to the upper layers.

Usually, microbial degradation offers the most significant, simpler, inexpensive and more environmentally friendly process of reducing environmental pollution from xenobiotic chemicals such as pesticides (Connell, 2005; Gavrilescu, 2005). For instance, white rot fungi Phanerochaete chrysosporium secrete a number of enzymes such as peroxidases, which have unique properties and abilities to degrade recalcitrant environmental pollutants such as DDT, polychlorinated biphenyl (PCB), benzo(a)pyrene (Shah et al., 1992).
Chemical Degradation and Transformation

Chemical degradation of pesticides is the abiotic transformation or breakdown of pesticides by different chemical reactions such as hydrolysis, oxidation-reduction and ionization, with the most important reaction being hydrolysis. Hydrolysis is the breakdown of molecular bonds of substances from reaction with water. The process may occur in soil solution or induced by hydration water on the surfaces of soil particles (Yaron, 1989; Gavrilescu, 2005). The hydrolytic process introduces a hydroxyl group that displaces a component of the molecules of the pesticide, leading to formation of smaller chemical groups. The products of this process become more soluble owing to the presence of the hydroxyl group and the small size of the molecular fragments; and may further be subjected to biotransformation. Also, the hydrolytic process changes the structure of the original compound, and most likely its properties. Consequently, the products of the reaction are usually less toxic than the original compound, although this is not always the case (Connell, 2005; Gavrilescu, 2005).

The rate of hydrolysis depends very much on the pH of the soil system because the process is commonly catalyzed by hydrogen or hydroxide ions (i.e. H⁺ and OH⁻, respectively) (Connell, 2005; Gavrilescu, 2005; Müller et al., 2007). The hydrolytic process is also influenced by temperature and microbial enzymes.

Photodegradation and Transformation

Photodegradation (photolysis) is the breakdown of pesticides upon exposure to light, principally, sunlight in the environment. This process may occur on the surface of soil, foliage, and in the air. Radiant energy in the form of photons excites the molecules of
the pesticide and causes various types of chemical reactions leading to the breakdown of the bonds of the molecules irradiated. There are two forms of photodegradation. These are direct and indirect photodegradation. With direct photodegradation, the photons are absorbed directly by the molecule being acted upon. However, in the case of indirect photodegradation, the molecule absorbs energy from another molecule that has absorbed the photons (Katagi, 2004; Gavrilescu, 2005).

Photodegradation is initiated by electromagnetic radiation in the range of 290 to 450nm, and the substance being acted upon must contain a chromophore which has the capacity to absorb solar radiation. The reaction rate is dependent on the light energy required for the process; available light intensity; the presence of inter-mEDIATE substances that facilitate indirect photodegradation; and the medium (Connell, 2005; Gavrilescu, 2005).

2.7.3 Movement Patterns in the Environment

Movement in the Air

Movement of pesticides away from the site of application by advective processes such as wind or air currents can be described as drift. Several factors determine how pesticides move in the air. These factors include volatility, vapor pressure, droplet size, wind, and temperature.

Volatility is the ability of liquid or solid substances to evaporate into gas and move freely with the air. Pesticides that are highly volatile easily evaporate upon contact with
air. For instance, fumigants are volatile and can therefore easily find their way into the atmosphere (Buttler et al., 2003; Gavrilescu, 2005). The volatility of a pesticide is impacted by its vapor pressure—the amount of pressure exerted by a substance at a particular temperature. At a given temperature, a pesticide with high vapor pressure is more volatile than pesticides with low vapor pressure. Henry’s Law coefficient (H) is used to describe the ratio of the partial pressure of a compound in air to its concentration in water. Pesticides with high H values tend to be more volatile than those with less value (Kookana et al., 2002; Connell, 2005; Gavrilescu, 2005).

Wind at high speed can carry airborne pesticides several kilometers away from the site of application. Pesticide particles in the air may be deposited onto surfaces beneath them when the velocity of the wind carrying them reduces and can no longer hold the particles (dry deposition). Deposition may also occur when rain droplets remove the pesticides particles from the atmosphere onto surfaces beneath (wet deposition) (Gavrilescu, 2005). Pesticide sprays with small droplet size are more likely to drift than large droplet sizes. This is because smaller droplets tend to remain buoyant in the air for a relatively longer time, and so can easily drift.

Air temperature inversions also affect the tendency for pesticides to drift. Air temperature inversion is a phenomenon which occurs when the air temperature near the soil surface becomes cooler than the air temperature above it. When this occurs, air near the ground lacks turbulence, therefore pesticide applied during this situation get highly concentrated in the air at or near the surface, providing a good condition for the pesticide droplets to drift away from their targets (Enz et al., 2014).
Movement in Water

Movement of pesticides in water is mostly by advective processes such as surface movement off the treated site (surface run-off) or by downward movement through the soil (leaching). Runoff and leaching usually occur when excess pesticide is applied or excess rainwater or irrigation water is applied, which carries the pesticide from the site (Randall et al., 2011). Also, the amount of a pesticide moved by surface runoff depends on its concentration in the few centimeters of surface soil (often 1-5 cm) (Kookana et al., 2002).

The solubility of a pesticide in water influences its tendency to move through or be moved by water. Solubility is a measure of the ability of a pesticide to dissolve in a solvent, which in environmental application is water. Pesticides that are highly soluble in water easily dissolve and may be carried away with water in surface runoff or move with water while percolating through the soil (Buttler et al., 2003). In contrast, less soluble pesticides are carried away in surface runoff attached to soil particles or sediment. Generally, herbicides are more soluble in water than insecticides or fungicides. They are therefore not easily sorbed and have greater mobility through soil (Kookana et al., 2002). Soil pH is one of the significant factors which can influence the solubility of some pesticides. An exception to this, however, is the case of DDT. Its solubility in water is not affected much by soil pH. Generally, pesticides that are likely to display an appreciable solubility in water are most likely to exhibit an increased solubility when exposed to acidic soils ) (Gavrilescu, 2005).
Movement in Soil

When a pesticide penetrates the soil, it may move through the soil interstitial spaces, attach to soil particles or be metabolized by soil organisms (Gavrilescu, 2005). Movement of pesticides in the soil is influenced by sorption-the process by which an organic compound in soil solution is taken up by the soil particles. The sorptive mechanisms that may operate in soils include ion exchange, cation bridging, charge transfer, hydrogen-bonding and van der Waals interactions (Kookana et al., 2002; Chen et al., 2013). Other processes such as degradation volatilization, hydrolysis, and photolysis depend on the sorption process (Müller et al., 2007).

Many factors impact on the sorption process in soil. Pesticides that are sorbed strongly to soil particles are less likely to be leached, and to reach ground water (Buttler et al., 2003). Moreover, pesticides with strong cationic characteristics (e.g. diquat and paraquat herbicides) are easily sorbed by the net negatively charged clay in soil. Thus, positively charged molecules are more strongly adsorbed to negatively charged soil particles (Kookana et al., 2002; Connell, 2005). However, the transportation of pesticides can be enhanced when they are sorbed to colloids (Kulikova and Perminova, 2002). This is because, colloids have the ability to move through the spaces between soil particles, and in the process, may carry with them any sorbed pesticide (Wan and K., 1997).

Also, the proportions of sand silt and clay in a soil or the distribution of soil particle sizes (soil texture), influences the movement of pesticides in the soil. Soils with more fine texture, such as clay, have a larger active surface area and lower water
permeability. There is therefore longer contact time and greater surface area for the sorption of pesticide cations (Sadler et al., 2001; Gavrilescu, 2005).

Another significant factor influencing sorption is the organic matter content of the soil. Soil organic matter may reduce the mobility of pesticides in two main ways. Humic substances (humic and fulvic acids) formed from soil organic matter have lipophilic properties with many polar and ionic sites, favoring the sorption of nonpolar and nonionic pesticides. Pesticides may also form complexes with the humic substances which are then sorbed onto the soil matrix (Connell, 2005; Müller et al., 2007; Chen et al., 2013). However, fulvic acids have been found to less effective in forming complexes with pesticides than humic acid (Lee and Farmer, 1989).
CHAPTER 3

LITERATURE REVIEW ON HUMAN HEALTH RISK ASSESSMENT OF CHEMICALS IN NATURAL AND OCCUPATIONAL ENVIRONMENTS

3.1 Background

Humans encounter chemical pollutants in their environments on daily basis, putting them at risk of exposure and adverse health and other effects. Health risk may be defined as the likelihood of an adverse effect occurring due to exposure to a chemical or other pollutants in the human environment (Connell, 2005). Health risk assessment has evolved over the years as a major tool to help identify, evaluate and manage risks from environmental pollutants, for the protection of both human health and the environment. Human health risk assessment may broadly be defined as the “process of estimating the potential impact of a chemical, physical, microbiological or psychosocial hazard on a specified human population under a specific set of conditions for a certain time frame” (DHA, 2012).

A common framework for health risk assessment of chemicals is the one proposed by the United States’ National Research Council (NRC) and adopted by United States Environmental Protection Agency (USEPA) (NRC, 2009; USEPA, 2014). The framework has undergone significant professional appraisal and has been found to be appropriate for most situations. In Ghana, the framework is widely accepted and has been applied in many studies to evaluate chemical pollutants (Obiri et al., 2010; Ansa-Asare et al., 2015; Bortey-Sam et al., 2015; Obiri et al., 2016). According to the framework, health risk assessment process is grouped into four main steps. These are hazard identification, dose-response assessment, exposure assessment, and risk
characterization. A diagrammatic representation of the framework is given in Figure 3.1. The risk assessment process helps to decide whether measures should be put in place to control risk (i.e. risk management). Risk management becomes necessary when the risk characterized is not “acceptable”. In the risk management process, different options are evaluated considering the social, political, economic, as well as the technological implications of the options (Gerba, 2000).

Figure 3.1: Health Risk Assessment Framework for Evaluating Chemical Pollutants
[adapted from NRC (2009)]
3.2 Hazard Identification

This is the first step involved in health risk assessment is to identify the possible hazard and qualitatively assess the ability of chemical agents to cause harm to humans through a review of the chemical and biological information of the agent (USEPA, 1995; Gerba, 2000). Such information may include physic-chemical properties; potential routes and patterns of exposure; quantitative structure-activity relationship; absorption, distribution, metabolism characteristics; and the influence of other toxicological effects. Such information is usually based on epidemiological data from human studies and toxicological data from laboratory experiments on test animals. The possible biological effect or harm caused by a chemical may include sub-lethal effects, such as alteration in respiration rate, growth retardation, and developmental deformities. At higher doses, the effect of pesticide exposure may be lethal (Connell, 2005). Generally, acute and chronic exposures will lead to different endpoints.

3.3 Dose-Response Assessment

This step involves an assessment of the dose-response relationship of a compound to evaluate the toxicity of a compound quantitatively. The concept of dose-response relationship describes the association between an observed adverse effect in humans or animals and the exposure dose environment (Connell, 2005). Hypothetical dose-response association is illustrated in Figure 3.2. This is a plot of the dose against the cumulative percentage responding. It is usually carried out on a homogeneous population of rats, mice, fish and other laboratory organisms.
Figure 3.2: Diagrammatic Illustration of a Dose-Response Relationship of Environmental Pollutants.

Dose-response relationships may be based on data from surrogate animal studies, human epidemiological studies, structure-activity relationships, and *in vitro* investigations (NRA, 2000; Connell, 2005). Data from human studies are regarded as the most appropriate option since they are more directly applicable to human populations, compared to data from animal studies. Humans differ considerably from surrogate animals in many characteristics. Also, the exposure doses used on experimental animals are usually much higher than the levels found in human environments. Data from animal studies may present difficulties in use for human health
risk assessment (Connell, 2005; Phung et al., 2015). However, statistically defined dose-response data is not available since experiments cannot be conducted on humans. In addition, human epidemiological studies are usually conducted on heterogeneous populations with variable exposure periods, diverse responses, and do not have quantified chemical exposure data (Connell, 2005).

The dose-response relationships may be used to obtain measures of toxicity such as No Observable Adverse Effect Level (NOAEL) or Lowest Observed Adverse Effect Level (LOAEL) (Figure 3.2) (Connell, 2005). An alternative measure of toxicity that may be obtained using the dose-response relationship is the benchmark dose (BMD). This is the “dose levels corresponding to specific response levels near the low end of the observable range of the data”. Often, 5% cumulative probability is used to set the BMD. A major advantage of BMD approach is that, it is a statistically defined value and is more reliable than the NOAEL or LOAEL (USEPA, 2012).

A Guideline Value is the limit of exposure, below which the possibility of harm is rare and above which harm becomes increasingly likely. Different terminologies may be used to refer to Guideline Values, depending on the route of exposure and the agency that derived it. For non-occupational exposures, terminologies such as Acceptable Daily Intake (ADI), Tolerable Daily Intake (TDI), Reference Dose (RfD), Reference Concentration (RfC) may be used, while for occupational exposures, Threshold Limit Values (TLV), Short-Term Exposure Limits (STEL) and Permissible Exposure Limit (PEL) may be used (DHA, 2012).
A conventional approach to establishing Guideline Values is by dividing the measures of toxicity (such as NOAEL, LOAEL, or BMD), obtained by experiments on surrogate animals, by Uncertainty or Safety Factors to account for uncertainties. Usually, uncertainties are introduced by extrapolating from animals to humans, intra-species variation, different exposure times, and different exposure levels (DHA, 2012). Thus,

\[ GV = \frac{\text{NOAEL}}{\text{SF}} \text{ or } \frac{\text{LOAEL}}{\text{SF}} \text{ or } \frac{\text{BMD}}{\text{SF}} \]  
Equation 3.1

where GV is the Guideline Value and SF, the Safety Factor.

The most commonly used safety factor is 100. This is comprised of 10 for interspecies variation where data on animal is used and another 10 for intra-species variation to account for variation in sensitivity from babies to aged people, male to female and so on. Additional safety factors may be applied depending on factors such as the quality of data and the endpoint used for the dose-response assessment. Generally, Safety Factors used to derive Guideline Values range from 10 to 10,000 (DHA, 2012).

An alternative approach to establishing Guideline Values is by constructing a probabilistic plot of lowest effect data to identify the exposure level that may not be harmful to a population. Generally, the threshold value obtained at the 5% cumulative probability level is accepted as the value below which no observable adverse effect may be expected, hence, may be regarded as the Guideline Value (Connell et al., 2003; Cao et al., 2011; Phung et al., 2015).
3.4 Exposure Assessment

An assessment of human exposure to pesticides is an important step in the process of quantifying the related health risks. Exposure may be described in two ways-external exposure and internal exposure. External exposure may be defined as the contact of a contaminant with the external boundary of humans, such as the skin for dermal exposure, epithelium of the gastrointestinal tract for ingestion, and the pulmonary epithelium or inhalation. Internal exposure, on the other hand, may be defined as the uptake of a contaminant beyond the external boundary and reaching the systemic circulation of the body (Semple, 2005; Van Engelen et al., 2007).

3.4.1 Routes of Exposure

Humans are exposed to pesticides in three principal ways- inhalation, ingestion and dermal routes (Figure 3.3). Depending on the setting, these exposure routes may be described as occupational exposures or environmental exposures. However, some routes are not exclusive to a particular setting. For instance, inhalation and dermal routes are both possible in occupational as well as non-occupational settings. Also, a person may be exposed to a pesticide simultaneously by more than one route. It may therefore be important to consider all possible routes in order to quantify the aggregate exposure of a pesticide to a particular person or group of persons. In fact, most humans are exposed to pesticides in the environment and occupational exposure is an additional set of routes, in the case of farmers and farm workers (Van Engelen et al., 2007).
3.4.2 Methods for Measuring Human Exposure to Pesticides

The level of exposure to pesticides may be obtained by using personal samplers to directly measure the concentrations at the point where the person comes into contact with the environmental medium containing the pesticide as well as the periods of exposure. Examples include the use of pumps and filters (C18 sorbent cartridges) to collect air samples near the breathing zone of farm workers; and absorbent skin patches to sample for dermal exposure. The strength of the direct measurement approach is that, it is usually simple and gives direct measurement as it occurs in a particular pathway during the monitoring period. However, the approach may be expensive, time consuming, and uncomfortable for study subjects (Sexton et al., 1995; Hoppin et al., 2006; Ngo et al., 2010).
Exposure assessments may also be carried out by using mathematical models to calculate the concentrations and amounts of chemical resulting from different pathways to the population based on plausible assumptions, available measurements, inferences and professional judgment (Sexton et al., 1995; Hoppin et al., 2006; Harris and Wells, 2007). For instance, the USEPA’s Pesticide Handlers Exposure Database (PHED) is a useful tool for first tier exposure assessments for pesticide mixers, loaders, applicators, and flaggers under different environmental, hygienic, and working conditions. The information provided by the database may be used to estimate future and previous exposures for individuals in epidemiologic studies (Krieger, 2002; Harris and Wells, 2007).

Based on the routes of exposure, pesticides may also be evaluated by using air sampling pumps for inhalation exposure and dermal dosimetry for exposures on the skin. Methods for assessing dermal pesticide exposure include whole body, patch and hand wiping techniques (Durham and Wolfe, 1962; Chester, 1993; Fenske, 1993). With the patch technique, about 10 ×10 cotton patches are placed on selected body regions of applicators during pesticide spraying. The patches are subsequently removed after spraying and analysed for pesticide residues. Exposure on a particular anatomical region, where a patch was placed, is extrapolated from the exposure level on the patch. There is therefore the tendency to under- or over-estimate exposure levels since pesticide deposition on the region may not be uniform. The hand wiping technique involves the use of cotton gauze with organic solvent to wipe the hands of applicators after spraying. The measured exposure therefore, does not account for exposure on other parts of the body. With the whole-body dosimetry, applicators wear overall garment with a hood, socks, and hand gloves to intercept pesticides residues on the body during
spraying. For a complete exposure assessment, the whole-body dosimetry may include use of personal monitoring pumps to evaluate inhalation exposure. The whole-body dosimetry therefore offers a better estimate of pesticide exposure since it requires less assumptions in estimating exposure levels (Fenske, 1993; OECD, 1997).

Another approach for estimating pesticide exposure is use of biomarkers. With this approach, the parent compound, its metabolite, or enzyme activity in appropriate biological matrices, such as urine and blood is measured. The measured biomarker is then used to “reconstruct” the level of exposure retrospectively. This is done with knowledge of the rate of intake, uptake, metabolism and route of excretion of the biomarkers (Sexton et al., 1995; Krieger, 2002; Lam and Gray, 2003; Hoppin et al., 2006; Ngo et al., 2010). For instance, 3,5,6-trichloropyridinol (TCP) is the major urinary metabolite of chlorpyrifos. This may therefore be used to estimate the level of chlorpyrifos exposure among farmers (Phung et al., 2012b). Likewise, acetylcholinesterase (AChE) inhibition in blood may be regarded as an indicator of exposure to organophosphate pesticides (Krieger, 2002). Pesticides and their biomarkers differ in the rate at which they are eliminated from the biological matrices. Therefore, timing for sampling of biological matrices is important in order to obtain accurate measurements (Ngo et al., 2010). A major advantage of the biomarker approach is that, it demonstrates the occurrence of exposure and uptake of a pesticide. Also, this approach integrates exposure over all pathways, therefore information on the pathways or routes of exposure need not be known however, one of the challenges with the biomarker method is that there is a lack of specific physiologically based pharmacokinetic models for many pesticides (Hoppin et al., 2006). Also, sampling can
be burdensome for pesticide applicators (Scher et al., 2007). In addition, the laboratory analysis procedures involved are often complex and expensive (Fenske and Day, 2005).

### 3.4.3 Quantitative Estimation of Human Exposure

Quantitative estimation of exposure involves measuring or calculating the amount of pesticide entering the human body resulting from a particular pathway. This process requires collection and analysis of parameters such as concentration, duration of exposure, frequency of exposure, and exposure pathway (Semple, 2005; Hoppin et al., 2006). A main aim of exposure assessment is to evaluate the level of exposure of a chemical agent to a population of interest (USEPA, 2000). The formula for estimating pesticide exposure depends on a number of factors including the exposure route and media. Using urinary metabolites, Absorbed Daily Dose (ADD) of a pesticide may be estimated using the following equation (Mage et al., 2004; Curwin et al., 2007):

\[
ADD \ (\mu g/kg/day) = \left[ C \times Cn \times CF \times R_{mw} \right] / BW
\]

where, ADD is Absorbed Daily Dose (µg/kg/d); C, concentration of the pesticide metabolite in urine per gram creatinine (µg/g creatinine); Cn, calculated mass of creatinine excreted per day (g/day); CF, correction factor of the pesticide; R\textsubscript{mw}, ratio of the parent pesticide to the molecular weight of the pesticide metabolite; and BW, body weight (kg).
To calculate the Lifetime Average Daily Dose (LADD), the following equation may be used:

\[
LADD \ (\mu g/\text{kg}/\text{d}) = \frac{[\text{ADD} \times \text{EF} \times \text{ED}]}{\text{AT}}
\]

Equation 3.3

where, ADD (µg/kg/d) is the total Absorbed Daily Dose; EF, exposure frequency (spray events or contact events/year); ED, exposure duration (42 working-years: for 18-60 year-olds; or 70 years for lifetime); and AT, averaging time (70 years x 365 days/year).

3.5 Health Risk Characterization

3.5.1 Conventional Risk Characterization Techniques

Risk characterization step integrates the information obtained from hazard identification, exposure assessment, and dose-response relationships to establish the level of risk to human population (USEPA, 2000; NRC, 2009). One main objective of risk characterization is to evaluate whether or not human exposure to a chemical hazard of interest in the environment exceeds an established guideline value (DHA, 2012). Conventionally, such evaluation for a non-carcinogenic chemical may be expressed as hazard quotient (HQ), with the following equation:

\[
\text{HQ} = \frac{\text{Exposure}}{\text{Guideline Value}}
\]

Equation 3.4

Using the above equation, risk of adverse effect may exist among the population if HQ is above unity, while HQ less than unity, may imply no or less probability of adverse
effects. HQ of less than unity is usually considered as “acceptable risk”. For multiple exposure pathways, the HQ for each pathway may be added as the measure for potential adverse effect. The value obtained this way is described as the Hazard Index (HI) (Gerba, 2000; DHA, 2012). Thus,

\[ HI = \sum HQ \]  

Equation 3.5

In contrast to the situation with non-carcinogenic substances, with carcinogens (and cocarcinogens), there is no threshold dose below which the likelihood of developing an adverse effect (i.e. cancer) is zero. The parameter used to express cancer risk is the cancer Slope Factor (SF) - i.e. the slope of the dose-response curve. SF is described as the upper-boundary estimate of the life-time probability of developing cancer due to exposure to a certain amount of a carcinogen. SF values for most carcinogens may be obtained from the Integrated Risk Information System (IRIS) database of USEPA. SF is derived by linearly extrapolating from the high dose range to zero in the dose-response curve of the chemical (USEPA, 1989). At low doses, the dose-response curve of carcinogens is assumed to be linear. Therefore, carcinogens with high SF are associated with high rates of occurrence of cancer (Gerba, 2000; USEPA, 2005). SF (mg/kg/day)^{-1} is expressed as:

\[ SF = CR/CDI \]  

Equation 3.6

where, CDI is the chronic daily intake (mg/ kg/day) and CR (unitless), cancer risk.

Thus,

\[ CR = SF \times CDI \]  

Equation 3.7
Cancer risk is obtained as a direct proportion of the population, which is usually expressed as 1 in $10^6$ or 1 in $10^3$.

### 3.5.2 Probabilistic Risk Characterization Techniques

Human health risk assessment process is based on the exposure levels of a contaminant and the dose-response relationships among the population of interest. Conventionally, risk characterization is done by using single estimates of exposure and guideline value to calculate a single value as the measure of risk. Risk is then characterized as the Hazard Quotient, the ratio of exposure dose to a defined guideline value (Section 3.5.1). A major advantage of the conventional approach is that, it is simple and easy to understand (DHA, 2012). In reality however, the exposure and dose-response relationship varies among members of a population. Consequently, risk calculated using this conventional approach usually fails to take into consideration, the variability and uncertainties associated with exposure as well as dose-response data. To deal with uncertainty, conservative assumptions are usually made to reasonably represent worse-case scenarios. However, such assumptions may over-estimate the actual risk (Sander et al., 2006; Xia et al., 2014).

Probabilistic Risk Assessment (PRA), which is a relatively recent technique for assessing health risks, provides a method to solve the problems associated with the conventional health risk assessment techniques. With this recent technique, exposure and dose-response data are described by probability distributions, which give a measure
of the variability and uncertainty of these input parameters. The risk calculated from such distributions will consequently be expressed in terms of probability distributions, rather than as a single value. Risks expressed this way are more informative and useful, because in practice, not all members of a population have the same level of risk to a particular hazard, as assumed by the conventional risk assessment techniques.

Different methods of conducting probabilistic risk characterization exist. These include the HQ using probabilistic data, Monte Carlo Simulation (MCS) and Overall Risk Probability (ORP) techniques. The HQ technique is the most basic of all PRA techniques. With the HQ technique, exposure and dose-response data are plotted on the same axis in the form of Cumulative Probability Distribution (CPD) curves (Figure 3.4).

![Figure 3.4: Illustration of Cumulative Probability Distribution (CPD) Curves of Exposure and Dose-Response Doses of a Chemical Pollutant.](image)
The risk is assessed from the region where the exposure and effects CPD curves overlap. Generally, the risk level increases as the two CPD curves get closer to each other. Risk may be characterized by comparing the exposure dose at the 95th percentile (high exposure), 50th percentile (medium exposure), 5th percentile (low exposure), or any percentile of interest to the adverse effect threshold dose. Usually, the adverse effect threshold dose is determined at the 5% percentile on the dose-response curve (Connell et al., 2003; Cao et al., 2011; Phung et al., 2013). Consequently, HQ may be expressed as HQ95/5 and HQ50/5 for exposure dose at the 95th and 50th percentiles, respectively.

Alternatively, the exposure dose at the various percentiles may be compared with guideline values established by regulatory agencies. In this case HQ may be expressed as HQ95/guideline, HQ50/guideline, or HQ5/guideline. Strictly, the variants of PRA described above are not “fully” probabilistic because variation and uncertainty in contaminant’s dose-response among the population still exist. Because of its probabilistic nature, this approach still offers a superior assessment of risk than the conventional HQ technique.

The MCS technique involves modeling of the exposure and dose-response data, assuming normal or log data distribution. This method allows for the approximation of the output distribution by drawing thousands of random values from the input distribution (Van Der Voet and Slob, 2007). The simulation produces outputs expressed as a probability distribution of the Hazard Quotient (HQ\text{MCS}) values for each level of exposure and response considered (Figure 3.5). The simulation can provide the
proportion of the HQ_{MCS} values that exceed unity. This measure is the area under the curve from the x-axis value of unity to infinity (Figure 3.5).

![Figure 3.5: Illustration of Probability Distribution of HQ_{MCS}. The blue area is the proportion of HQ_{MCS} less than unity, while the red area is the proportion of HQ_{MCS} exceeding unity (adapted from Phung et al. (2013)).](image)

With the ORP method, CP exposure exceedance values are calculated using the expression \(1 - CP_{\text{exposure}}\) and plotted against the percentage of affected population (i.e CP_{\text{effects}} values) to obtain an ORP curve as illustrated in Figure 3.6. The overall risk probability is quantified as the area under the ORP curve. The area may be calculated as the product of the values for CP_{exposure} and CP_{effect} and it ranges from 0 to 100%. The risk increases as the curve moves further away from the origin of the graph (Solomon et al., 2000; Cao et al., 2011). The proportion of the population that may be adversely affected by any level of exposure exceedance can be determined from the plot.
PRA is widely accepted and has therefore been applied in many instances to assess risks to different chemical pollutants, including pesticides (Phung et al., 2013; Marasinghe et al., 2014), chlorinated disinfection by-products (Hamidin et al., 2008), endocrine disrupting chemicals (Cao et al., 2011), nitrate (Sadler et al., 2016), benzene, toluene and xylene (Edokpolo et al., 2014).

In summary, PRA gives a much more quantitative characterization of variability and uncertainties, and thereby less likely to include bias in risk outputs than the conventional single-point method. Also, the technique allows the flexibility of predicting risks for any change in the input parameters. Moreover, various remedial options for managing risks could be easily compared.
CHAPTER 4
METHODOLOGY

4.1 Conceptual Framework of the Research

This chapter presents the strategies used to achieve the objectives of the research. The research was based on the four-step health risk assessment framework proposed by the United States’ National Research Council (USEPA, 2000; NRC, 2009). Thus, the research involved hazard identification, dose-response assessment, exposure assessment and risk characterization (Figure 4.1). In addition, risk management strategies were proposed.

The objective of the hazard identification step (Section 4.4) was to identify the main types of hazardous pesticides used by the farmers. Other objectives were to assess pesticide exposure risk factors and the prevalence of self-reported pesticide poisoning symptoms among the farmers. With the exposure assessment step (Section 4.5 and 4.6), dermal and urine sampling were carried out to quantify the levels of exposure to chlorpyrifos, which was identified as the main type of pesticide used by the farmers. During the dermal and urine sampling, field factors were observed and documented (Section 4.7). The dose-response assessment step (Section 4.8) involved quantitative description of the relationships between chlorpyrifos exposure and resulting adverse effects through evaluation of Toxicant Sensitivity Distributions (TSDs) and a review of guideline values set by national and international agencies. The risk characterization step (Section 4.9) was then carried out to evaluate the probability of adverse effects occurrence among applicators, through integration of the information obtained from the
exposure assessment and dose-response steps. Lastly, strategies were proposed to help manage the levels of exposure and health risks quantified.

Figure 4.1: Conceptual Framework of the Research
4.2 Study Location and Population

The study was carried out among rice farmers of Kpong Irrigation Scheme (KIS) in Ghana. KIS is the second largest irrigation scheme for rice production in Ghana (ADF, 2005). The coverage area of KIS is situated about 80 kilometres (km) northeast of the capital city of Ghana, Accra. The area lies along the right bank of the Volta River stretching from Akuse to Asutsuare over a distance of about 20 km. The scheme has a developed land area of 3,452 hectares (ha) out which 1,870 ha and 1,400 ha is used for rice and banana cultivation, respectively. There are about 2,840 rice farmers in the scheme with an average farm size of about one hectare (KIS, 2013). The average farm size, however, is decreasing in recent times due to increasing demand for land by farmers with consequent re-distribution (Takeshima et al., 2013).

Figure 4.2: Study Location and a Typical Farmer Spraying Pesticide
4.3 Recruitment of Study Participants

Prior to recruitment of participants, the researcher met with key officers of the District Directorate of Food and Agriculture of Shai-Osudoku as well as the Project Management Unit of Kpong Irrigation Scheme to seek for permission to carry out the study in their area of jurisdiction. During these meetings, the objectives and activities of the study were explained. Contacts of the Agricultural Extension Officers (AEOs) and Technical Officers (TOs) of the scheme were also obtained by the researcher to arrange for meetings. The researcher had a series of meetings with the AEOs and TOs to seek their support and collaboration for the data collection since they have direct contact with farmers of the area. The AEOs and TOs assisted the researcher to identify participants for the study and served as data collection assistants.

Farmers were visited in various places including farms, homes, rice drying platforms, rice mills, and at social functions. With the support of the AEOs and TOs, the researcher explained the objectives, activities and benefits of the study to potential participants. Collection of primary data for the study involved four main approaches, namely, questionnaire interview, field observation, dermal sampling as well as urine sampling. Farmers who agreed to participate in the study and satisfied the inclusion criteria below were asked to indicate the data collection approach (es) they were willing to be involved with. To be included, rice had to be the main crop grown by the farmer and the farmer had to be at least 15 years of age (the minimum legal working age in Ghana). Participant Information Sheet (Appendix 1) detailing the study objectives, procedures, requirements of the study participants, among others were explained to the participants in both English and the local languages. This was done with the support of
the local members of the communities. Farmers who expressed their willingness to participate in the study were given copies of the Participant Information Sheet. They were then asked to sign Informed Consent Form (Appendix 2). The protocols for the study were reviewed and approved by Ghana Health Service Ethical Review Committee (GHS-ERC: 10/07/15) and Griffith University Human Ethics Committee (GU Ref. No: ENV/24/15/HREC).

A convenient time and place were arranged for the farmers to complete the questionnaire. The respondents to the questionnaire who were also prepared to participate in the field observation, dermal and urine sampling activities were later contacted to obtain their pesticide spraying schedules for the research team to plan for these activities.
4.4 Hazard Identification among Rice Farmers in Ghana with Questionnaire

4.4.1 Development of Questionnaire

A questionnaire (Appendix 3) was developed to collect information among a cross section of farmers in the study area. The questionnaire sought to obtain information on four main aspects. These were socio-demographic characteristics; pest control and pesticide use; pesticide exposure risk factors; and self-reported pesticide poisoning symptoms. The list of symptoms included in the questionnaire was guided by the WHO’s standard case definition of Acute Pesticide Poisoning (Thundiyil, 2008) as well as its Pesticide Poisoning Surveillance Questionnaire (WHO, 2009a). In addition, questionnaires developed for similar studies (Clarke et al., 1997; Jørs et al., 2006; Jensen et al., 2011) were also consulted. The items of the questionnaire were reviewed and refined by all four members of the supervisory team of the study. Information obtained from the interview is important in understanding the risks factors of pesticide exposure and for making well informed recommendations to address those factors.

4.4.2 Pilot Testing of Questionnaire

A pilot testing of the questionnaire was carried out among 20 farmers to further refine it, prior to its use in the main study. During the pilot testing, the research team obtained feedback from the farmers on issues such as their ease of understanding the questions, their comfort with the questions and the time spent in responding to the questions. Responses obtained from the pilot testing were entered into a Statistical Package for the Social Sciences (SPSS) database. These exercises enabled the researcher to identify the
problems with some of the questions which were then amended. The amendments mainly involved re-wording of some of the questions, revising some of the response options, and adding/deleting some questions. The pilot testing also enabled the research team to identify the best places and times of the day to meet farmers for recruitment and administration of the questionnaires.

4.4.3 Data Collection

Face-to-face interviews using the structured questionnaire which had been developed were conducted among 214 participants out of about 2,840 rice farmers, representing 7.5% of farmers in the study area. Similar previous studies suggest that the sample size used in this study is representative of the farmer population (Clarke et al., 1997; Jørs et al., 2006; Oesterlund et al., 2014).

The study was carried out from 1st November to 30th December 2015. The Convenient Sampling Method (Etikan et al., 2016) was adopted to select participants for the study. This sampling approach has the potential to introduce selection bias. To minimise bias, efforts were made by the research team to sample participants across a large number of communities within the study location. The convenient sampling method is useful in the context of developing countries because of non-existence of registers for persons, inadequate house address systems, as well as bad road networks (Oesterlund et al., 2014). These situations make the use of more appropriate sampling approaches such as random sampling, difficult. The convenient sampling approach has been used in similar studies (Clarke et al., 1997; Khan et al., 2014; Oesterlund et al., 2014).
4.4.4 Data Analysis

Data obtained from the questionnaire interview were checked for completeness, coded and entered into an SPSS spreadsheet (version 20). The analysis performed were descriptive and consisted of frequencies, proportions, means and standard deviations of the variables investigated. Cases with incomplete data were not included in the analysis.

4.5 Assessment of Dermal Exposure to Chlorpyrifos Based on Whole-Body Dosimetry

4.5.1 Principle of the Procedure

The dermal route is the most important pathway by which pesticide applicators are exposed with the back-pack spraying method of application (Dowling and Seiber, 2002; Damalas and Eleftherohorinos, 2011; Fenske et al., 2012). It may account for about 94-96% of pesticide exposure in occupational settings (Fenske et al., 2012). Dermal exposure assessment approach may therefore be applied to evaluate the exposure levels of chemical pollutants that enter the body through dermal absorption. Dermal exposure assessment could yield results that are comparable to estimates from biomonitoring techniques (USEPA, 2007b; Ross et al., 2008). In addition, dermal exposure assessment techniques help to establish the pathways of exposure, which are useful in prescribing appropriate protective measures to help reduce the risk of exposure (Frenich et al., 2002; Albertini et al., 2006). Moreover, dermal exposure assessment techniques are usually less expensive and may therefore be more practical with limited budget in resource-poor countries (Sexton et al., 2004).
Methods for assessing dermal pesticide exposure include whole-body dosimetry, patches, chemical removal, and fluorescent tracer techniques (Durham and Wolfe, 1962; Chester, 1993; Fenske, 1993). However, the whole-body dosimetry technique offers a better estimate of dermal pesticide exposure since it requires fewer assumptions in the estimation process (Fenske, 1993; OECD, 1997). In this research, the whole-body dosimetry technique was used to sample chlorpyrifos residues from applicators to evaluate the levels, patterns, and determinants of dermal exposure in the present study. The technique was based on the protocols of the Organisation for Economic Co-operation and Development and World Health Organisation (WHO, 1982; OECD, 1997).

4.5.2 Dermal Sampling Procedure

On the day of spraying, each applicator was given a new set of Tyvek overall under-wear garment made of flash-spun, high-density polyethylene (DuPont™ Tyvek®), white cotton hand gloves, and socks (Figure 4.3). These sampling media were worn by the applicators with their usual farm clothes worn over the sampling media before beginning of any pesticide spraying activity (Figure 4.4). The purpose of this sampling procedure was to capture pesticide residues that penetrated applicators’ clothing during spraying activities and potentially reaching their skin, as well as residues adhering to body areas of the applicators not covered by their farm clothing. These exposed areas included the face, neck, hands and feet. Tyvek under-wear garments and cotton sampling media have been found to satisfactorily trap and retain chlorpyrifos-methyl (Castro Cano et al., 2000) and other organophosphate insecticides (Castro Cano et al., 2001; Machera, 2003).
Figure 4.3: A Sample of the Tyvek Garments, Socks, Hand Gloves, and Gauze used for Sampling.

Figure 4.4: Applicator Wearing Sampling Media

A: Applicator wearing Tyvek coverall
B: Applicator wearing farm clothes over Tyvek coverall. Also worn are hand gloves and socks
C: Applicator applying pesticide wearing farm clothes over Tyvek coverall
Immediately after spraying, the Tyvek underwear garment and the rest of the sampling media were carefully removed from the applicators and dissected into nine anatomical regions (Figure 4.5). The head, front abdomen, back abdomen, upper arms, lower arms, hands, upper legs, lower legs, and the feet were labelled as 1, 2, 3, 4, 5, 6, 7, 8, and 9, respectively. The face and neck of each applicator were wiped with 2 pieces of 8-ply dry sterile surgical cotton gauze (10 cm by 10 cm) and added to the sampling media of the head section (anatomical region 1). Each section was folded, wrapped with aluminium foil, placed in a pre-labelled zip-lock plastic bag and then kept in an ice chest packed with ice, away from direct sunlight. The label on the bag consisted of the code of the applicator, anatomical region, and the date of sampling. The samples were transported to the laboratory within one hour and stored at -25°C until analysed.

Figure 4.5: Tyvek Underwear Garment, Hand Gloves and Socks Sectioned into Nine Anatomical Regions.
4.5.3 Extraction of Tyvek Under-Wear Garments, Cotton Hand Gloves, Socks and Gauze

The extraction and analysis of the samples for chlorpyrifos were carried out at the Pesticide Residues Laboratory of Ghana Standards Authority using a modified version of the analytical methods for agricultural chemicals of Japan’s Department of Food Safety (DFS, 2006). The pesticide sampling media (Tyvek garments, cotton hand gloves, socks and gauze) were placed in pre-washed glass bottles of various volumes depending on the size of the sampling media. Pesticide grade ethyl acetate (Fisher Scientific, UK) (150mL to 1,150mL) was then added to each sample until fully submerged. The bottles were placed in ultrasonic water bath (Decon FS400B) and sonicated for 45 minutes at room temperature (25°C). The extracts were then filtered with anhydrous sodium sulfate (5g) (Glass World, South Africa). Aliquots of the extract (70 to 200mL, depending on the quantity of the initial volume) were taken and concentrated with a rotary evaporator (Büchi Rotavapor R-210, USA) at 39°C at 79 mbar to dryness. The residues were redissolved with ethyl acetate (1 mL) and transferred to vials (2 mL) for Gas Chromatography (GC) analysis. After sectioning, the dermal samples obtained from 20 of the applicators were analysed as one composite sample for each applicator, while samples from the remaining four applicators were analysed separately according the anatomical regions shown in Figure 4.5.

4.5.4 Analysis for Chlorpyrifos

A Varian CP 3800 Gas Chromatograph (Varian Associates Inc, USA) equipped with Pulsed Flame Photometric Detector (PFPD) and a CombiPAL auto sampler was used
for the analysis. Chromatographic separations for chlorpyrifos were performed with a capillary column coated with VF-1701ms (30 m, 0.25 mm, 0.25 μm film thickness). The carrier gas was nitrogen at a flow rate of 2.0 mL/min, while hydrogen (14 mL/min), air 1 (17 mL/min) and air 2 (10 mL/min) were used for the detector. The injector (splitless mode) and PFPD temperatures were held at 270°C and 300°C, respectively. The column oven temperature was programmed as follows: 70°C for 2 minutes, increased steadily at a rate of 25°C/minutes to 200°C, then at 20°C/minutes up to 250°C and held for 4.3 minutes. The injection volume was 2.0 μL and the total run time for each sample was 15 minutes. Instrument control, data acquisition and processing were done with the Star Chromatography Workstation software (Version 6.4.1).

Chlorpyrifos standard (Dr. Ehrenstorfer GmbH, Germany) calibration mixtures were prepared for PFPD detection at six concentration levels in ethyl acetate (0.01, 0.02, 0.05, 0.10, 0.50 and 1.0 mg/L). These were run in the GC to obtain their corresponding peak areas. The calibration mixtures with the corresponding peak areas were used to derive a calibration curve with R² value of 0.99. The peak areas of the samples were used to calculate the respective concentrations. Further dilution of the extracts was done, when appropriate, to ensure that the concentrations were within the linear range of the calibration curve. The concentration of chlorpyrifos in each extract and the final solution volume after preparation for GC analysis were used to calculate the mass of chlorpyrifos residues in the sampling media.

Sample matrices were spiked with standard chlorpyrifos at 0.05 mg/L and analyzed with each extraction batch. The recovery rates (%) from the spiked matrices were 94%, 88%,
88%, and 96%, for Tyvek garment, cotton socks, cotton hand gloves, and cotton gauze, respectively. The quantities of chlorpyrifos obtained were adjusted based on the recoveries of the spiked samples. The Limit of Detection (LOD) and Limit of Quantification (LOQ) were determined using the formulae, LOD = S × t and LOQ = S × 10, where, S is the standard deviation of the replicate analysis, and t, the student’s t-value for the 99% confidence interval with n-1 degrees of freedom (Wisconsin Department of Natural Resources, 1996; USEPA, 2012). The limit of detection and limit of quantification were determined to be 0.005 mg/L and 0.01 mg/L, respectively.

4.5.5 Quality Control

Quality control and quality assurance measures consisted of solvent blanks, matrix blanks, and standards which were analyzed alongside each extraction batch and found to be satisfactory. To ensure high laboratory testing and calibration standards, the Pesticide Residues Laboratory of Ghana Standards Authority participates in international accreditation schemes. It is ISO/IEC 17025:2005 compliant and accredited by Deutsche Akkreditierungsstelle GmbH (DAkks) for analysis of organophosphate insecticides including chlorpyrifos, with certificate No. D-PL-15209-01-02.

4.5.6 Calculation of Dermal Exposure

The magnitude of dermal exposure was measured by three parameters: Total Dermal Exposure (TDE, mg), Unit Exposure (UE, % active ingredient handled), and Skin Loading (SL, µg/cm² of skin area). TDE was calculated as the sum of the chlorpyrifos
obtained from all sections of the body (head, front abdomen, back abdomen, upper arms, lower arms, hands, upper legs, lower legs, and the feet) for each applicator. To determine the proportion of the active ingredient that the applicators were exposed to, UE was calculated by expressing TDE as a percentage of the quantity of Active Ingredient (AI) applied by each applicator [UE % = (TDE mg / AI mg) × 100]. SL was calculated to evaluate the level of exposure per unit skin area by expressing TDE for each anatomical region as a ratio to the skin surface area of the respective anatomical region. The average (±SD) skin surface areas of the anatomical regions determined and applied were as follows: head (1,200 ± 54 cm²), front abdomen (3,950 ± 125 cm²), back abdomen (3,950 ± 120 cm²), upper arm (1,700 ± 82 cm²), lower arm (1,200 ± 67 cm²), hands (680 ± 25 cm²), upper legs (2,300 ± 62 cm²), lower legs (2,000 ± 43 cm²) and feet (750 ± 22 cm²).

4.5.7 Selection of Chlorpyrifos Dermal Absorption Factor (DAF) for Calculating Absorbed Dose from Dermal Exposure

Dermal absorption of chemicals may be defined as the entry of a chemical agent (such as pesticides) across the skin barrier of exposed individuals. Through dermal absorption, a chemical agent may reach one or more organs of the body, causing adverse health effects (USEPA, 2007a). Many factors affect the rate of dermal absorption of chemicals. These include perspiration (Williams et al., 2004), physiochemical properties of the pesticide, concentration, exposure frequency, duration, vehicle, formulation type (Ngo et al., 2010) and “inert” ingredients (Baynes and Riviere, 1998; Cox and Surgan, 2006).
Dermal Absorption Factor (DAF) provides a measure of the rate at which pesticides can be absorbed into the skin. Thus, the DAF provides an index of dermal pesticide exposures. Consequently, DAFs have been established for pesticides for purposes of exposure and health risk assessment. These DAFs have been determined mainly through experimental *in vivo*, *in vitro* as well as Quantitative Structure–Activity Relationship (QSAR) studies (Ngo *et al.*, 2010). However, results from *in vivo* studies are more acceptable because they are believed to give more accurate outcomes since they are based on direct measurement (Zendzian, 1994; Mueller *et al.*, 2008).

In *in vivo* pesticide dermal absorption studies, a certain quantity of the pesticide is applied over a defined area of the skin of study subjects. The quantities of the metabolite or the parent compound of the applied pesticide is then measured in body fluids such as the urine and blood, after a specified period of time. The quantity recovered is used to estimate the absorbed dose and then expressed as a percentage of the original dose applied on the skin, to obtain the DAF. Thus, DAFs may be mathematically expressed as:

\[ \text{DAF} \, (\%) = \left( \frac{\text{Estimated Absorbed Dose}}{\text{Applied Dermal Dose}} \right) \times 100 \]  
Equation 4.1

The DAF proposed for chlorpyrifos by different authors, ranges from 1 to 9.6% (Nolan *et al.*, 1984; Thongsinthusak, 1991; Griffin *et al.*, 1999; Geer *et al.*, 2004; Meuling *et al.*, 2005). The variation in the DAF values could be due to variations in the experimental parameters such as the dose applied, vehicle used and duration of exposure (Ngo *et al.*, 2010). An assessment of the basis for arriving at the different
DAF values is therefore necessary to decide on the most appropriate DAF to apply. Consequently, the following criteria were used to identify studies evaluating DAF of chlorpyrifos:

- primary study
- published in scientific peer reviewed journal;
- used acceptable experimental technique; and
- conducted with human subjects.

The parameters of the studies identified are summarized in Table 4.1. A major difference in the experimental parameters among the studies is the levels of chlorpyrifos applied to the skin. The exposure levels in the studies by (Nolan et al., 1984) and (Griffin et al., 1999) are problematic. This is mainly because the levels (4,160 µg/cm² and 367 µg/cm², respectively) are much higher than the levels found in field conditions, which range from 1 to 25 µg/cm² (Thongsinthusak et al., 1999; Meuling et al., 2005). As with many other compounds, the percentage of absorbed dose of chlorpyrifos is inversely proportional to the applied exposure level, when the limit of the absorptive capacity of the skin is reached (Thongsinthusak et al., 1999; Meuling et al., 2005; Mueller et al., 2008; Ngo et al., 2010). The DAF of the studies by (Nolan et al., 1984) and (Griffin et al., 1999) may have therefore, under-estimated the skin absorption rate for chlorpyrifos. Another major difference in the parameters used in the DAF experiments is the duration of exposure, which ranged from 4 to 20 hours. The duration of the experiments by (Griffin et al., 1999) (8 hours) and Meuling et al. (2005) (4 hours) are typical of those found in field conditions. However, the exposure duration of the
experiment by (Nolan et al., 1984) (12 to 20 hours) can be more than what apply in typical field conditions.

With the present study, the DAF proposed by Meuling et al. (2005) was regarded more appropriate considering the applied dose (50 µg/cm²) and duration (4 hours) of the experiment, which were closer to the spraying characteristics of the present study (applied dose of 0.3 to 13 µg/cm² and spray duration of 0.4 to 1.8 hours (Atabila et al., 2017).

Table 4.1: Summary of Studies on Dermal Absorption Factor for Chlorpyrifos in Humans

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of study subjects</td>
<td>6</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Anatomical site</td>
<td>Volar surface of the forearm</td>
<td>Volar surface of the forearm</td>
<td>Volar surface of the forearm</td>
</tr>
<tr>
<td>Applied dose/quantity (µg /cm² of skin)</td>
<td>4,160</td>
<td>367</td>
<td>50</td>
</tr>
<tr>
<td>Exposure duration(hours)</td>
<td>12 to 20</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Percentage of applied dose/quantity washed off after exposure duration</td>
<td>Not determined</td>
<td>53</td>
<td>42</td>
</tr>
<tr>
<td>Solvent/vehicle</td>
<td>Dipropylene glycol methyl ether or methylene chloride</td>
<td>Water</td>
<td>Ethanol</td>
</tr>
<tr>
<td>Sampling media</td>
<td>Urine</td>
<td>Urine and blood</td>
<td>Urine</td>
</tr>
<tr>
<td>Sampling period (hours)</td>
<td>120+</td>
<td>100</td>
<td>120</td>
</tr>
<tr>
<td>Metabolite analysed</td>
<td>TCP</td>
<td>TCP</td>
<td>TCP</td>
</tr>
<tr>
<td><strong>Dermal Absorption Factor (%)</strong></td>
<td><strong>1.28±0.8</strong></td>
<td><strong>1±0.4</strong></td>
<td><strong>4.3±1.4</strong></td>
</tr>
</tbody>
</table>
4.5.8 Calculation of Absorbed Daily Dose (ADD\textsubscript{D}) and Lifetime Average Daily Dose (LADD\textsubscript{D}) of Chlorpyrifos from Dermal Exposure

Using the TDE data of the applicators, Absorbed Daily Dose (ADD\textsubscript{D}) of chlorpyrifos from dermal exposure was estimated with the following equation:

\[
\text{ADD}\textsubscript{D} = \frac{(\text{TDE} \times \text{DAF})}{\text{BW}} \quad \text{Equation 4.2}
\]

where, ADD\textsubscript{D} is the dermal Absorbed Daily Dose (µg/kg/day); TDE, Total Dermal Exposure (µg/day); DAF, Dermal Absorption Factor (4.3 %) (Meuling \textit{et al.}, 2005); and BW, Body Weight of each applicator (kg).

Lifetime Average Daily Dose (LADD\textsubscript{D}) of chlorpyrifos from dermal exposure with the applicators was estimated with the following equation:

\[
\text{LADD}\textsubscript{D} = \frac{(\text{ADD}\textsubscript{D} \times \text{EF} \times \text{ED})}{\text{AT}} \quad \text{Equation 4.3}
\]

where, ADD\textsubscript{D} (µg/kg/day) is the dermal Absorbed Daily Dose of chlorpyrifos of the applicator; EF, the Exposure Frequency (Number of days per year); ED, the Exposure Duration (Work lifetime years); and AT, the Averaging Time [(life expectancy in years – application start age in years) x 365 days/ year].
4.5.9 Data Analysis

General descriptive statistics determined to summarize the variables investigated were frequencies, proportions, means, standard deviations and ranges. In addition, TDE and UE were described with Cumulative Probability Distribution (CPD) plots, which were obtained using Microsoft Excel. The Cumulative Probabilities (CPs) of TDE and UE values were calculated using the equation below, after ranking the data points from the lowest to the highest:

\[
CP(\%) = \frac{(i/n+1) \times 100}{100}
\]

Equation 4.4

where, CP is cumulative probability (%), i, the \(i^{th}\) point and n, the total number of data points.

CPD plots allow the flexibility of determining the exposure level at any percentile of interest. Also, with the use of the Statistical Package for the Social Sciences (SPSS) (Version 20), the association between TDE and independent variables were assessed with independent t-test.
4.6 Assessment of Overall Exposure to Chlorpyrifos Based on Urinary 3,5,6-Trichloro-2-Pyridinol (TCP)

4.6.1 Principle of the Procedure

Some chemical pollutants produce specific metabolites which are excreted through bodily fluids such as urine and blood of exposed persons. Exposure to such toxicants may be assessed based on the urinary concentration of their metabolites, with knowledge of the pharmacokinetic properties of the toxicants (Barr and Angerer, 2006; Hoppin et al., 2006; Tan et al., 2012). This approach gives an index of the actual absorbed dose due to exposure compared to environmental monitoring approaches such as dermal dosimetry, that evaluate potential absorbed dose (OECD, 1997; Albertini et al., 2006; Fustinoni et al., 2014). The approach also takes into account exposures from all routes and therefore presents an overall measure of exposure (Albertini et al., 2006; Barr and Angerer, 2006).

The compound 3,5,6-trichloro-2-pyridinol (TCP) is a specific biomarker of the insecticide chlorpyrifos (Figure 4.6). The biomarker is found mainly in the urine of exposed persons. Analysis of urinary TCP to estimate chlorpyrifos exposure among individuals have been carried out in a number of studies based on 24-hour urine sampling (Saieva et al., 2004; Baker et al., 2005; Phung et al., 2012b). Compared to other sampling methods such as spot urine sampling, the 24-hour sampling gives a better estimate of exposure dose because there is less room for estimation error (Barr and Angerer, 2006; Scher et al., 2007; Bradman et al., 2013).
In this study, the 24-hour urine sampling method was used to obtain urine samples from participants of the study. The samples were analysed for both TCP and creatinine which were used to estimate chlorpyrifos exposure dose among the applicators.

### 4.6.2 Urine Sampling Procedure

This exposure assessment study was based on a single pesticide spraying event for each applicator. All the applicators of the study sprayed rice crops with chlorpyrifos (Dursban - 480g/L Emulsifiable Concentrate), using hand-pressurized knapsack spraying devices that were carried on the back. Information such as Personal Protective Equipment (PPE) usage, type of clothing worn, spraying duration, quantity of insecticide applied, number of spray tanks, crop height, farm size, as well as incidences of spills, and leakages were observed and recorded during the spray event.
Prior to sampling, the applicators were given a one-day training session on self-sampling procedures for taking 24-hour urine samples. In the evening preceding the sampling days, each applicator was given a set of sampling items, which comprised an ice chest (8 L), ice packs, and a plastic jar (2 L) to keep the urine samples at 4°C. Each applicator was required to submit six urine samples collected over 24-hour periods, which included one sample before the spraying day (background sample), one sample during the spraying day, and four samples at 24-hour intervals after the spraying day (post-application samples). Sampling for each spraying day began with the first void after spraying had begun until the same time of the subsequent day. The applicators were requested not to apply chlorpyrifos for at least one week prior to the first sampling day and another week after the spraying day. They were also encouraged not to leave the study area during the sampling period in order to capture all urine voids within each 24-hour period.

All the samples were delivered to the laboratory at Osudoku Health Centre, located in the community where the applicators were based. Three aliquots were taken from each sample and stored in HDPE bottles (60 mL). All of the samples were transferred to the Pesticides Residues Laboratory of Ghana Standards Authority (GSA) in Accra and stored at -25°C. One set of the aliquot samples was sent later to Patholab Solutions Ghana Limited in Accra and analysed for creatinine. The second set was shipped with dry ice (20 kg) by air to Queensland Health Forensics and Scientific Services (QHFSS) in Brisbane for TCP analysis. On receipt, an acceptable quantity of dry ice remained in the containers. At QHFSS, the samples were stored at -25°C until analysis. The third set of the aliquot samples remained with the Pesticides Residues laboratory of Ghana Standards Authority as a reserve.
4.6.3 Sample Extraction and Analysis of Urinary TCP

Sample extraction and analysis was performed by Queensland Health Forensic and Scientific Services (QHFSS, Brisbane, Australia), a National Association of Testing Authorities laboratory accredited to International Organisation for Standardisation 17025 standards for chemical testing. Aliquots of urine (1 mL) were spiked with isotopically labelled TCP (13C5-TCP, Toronto Research Chemicals, Toronto, Canada), adjusted to pH >12 with 10M NaOH and heated at 60°C for two hours. The samples were then adjusted to pH < 3 with 42.5% w/w H3PO4 and 0.45 µm filtered (13mm Phenex RC, Phenomenex, Torrance, USA). The prepared samples were analysed by liquid chromatography coupled with tandem mass spectrometry in positive ESI mode on a Shimadzu Prominence UFLC (Kyoto, Japan) coupled to an Applied Biosystems API 4000 mass spectrometer (Framingham, USA) using a Kinetex C18 column (50x2.1mm, 5µm, Phenomenex, Torrance, USA) and a 1% to 95% methanol gradient with 0.1% acetic acid. The TCP instrumental analysis was performed solely by QHSS staff.

4.6.4 Quality Control for Urinary TCP Analysis

Quality control consisted of duplicate samples, spiked samples, conjugate spiked samples, blank samples, spiked blank samples, and conjugate spiked blank samples run every 20th sample. Synthetic urine, as per Method 6301.02 of the Centre for Disease Control and Prevention (CDC), was used as the blank matrix. Conjugate spiked samples were spiked with TCP Glucuronide (Carbosynth, Compton, UK) to monitor hydrolysis performance. TCP for spiked samples and standards was sourced from Dr. Ehrenstorfer GmbH (Augsburg, Germany).
4.6.5 Sample Extraction and Analysis for Urinary Creatinine

Creatinine is a metabolic waste product of creatine and creatine phosphate which is formed in muscle tissues (Barr et al., 2005; Mage et al., 2008). Urinary creatinine levels in humans range from 1.0 to 2.5 g per day (Campins Falco et al., 2001), depending on factors such as age, gender, body height, body weight, lean muscle mass, and the level of physical activity (Knight et al., 2004; Baxmann et al., 2008). The rate of formation and excretion of creatinine in an individual is relatively constant and excretion is mainly through the urine (Barr et al., 2005; Peters et al., 2014).

A challenge associated with the measurement of chemical toxicants or their metabolites in urine sample is the daily variation in urine volume which may affect concentration of the toxicants or metabolites being investigated. An approach applied to compensate for urine variation is to normalize the urinary concentration of the toxicant in relation to the concentration of creatinine in the urine in order to obtain a more accurate measurement (Barr et al., 2005; Cocker et al., 2011). This is attained by dividing the urinary concentration of the toxicant (in µg/L urine) by the urinary concentration of creatinine (g/L urine), which converts the unit of the toxicant to µg/g creatinine. Accordingly, urinary creatinine concentrations were determined and used to compensate for urine variation, in determining the urinary TCP concentrations of the applicators in the present study (Section 4.6.7).

Determination of creatinine was based on the kinetic Jaffe reaction colorimetric method. With this method, creatinine combines with alkaline picrate solution to form an orange-red complex. The light absorbance of this complex, which is proportional to the
creatinine concentration, is measured and used to estimate the levels of creatinine
(Campins Falco et al., 2001; Mohabbati-Kalejahi et al., 2012). Aliquots of urine were
transferred into plastic test tubes and spun obtain a clear urine sample. A dilution (1 in
50) was made in distilled water for the analysis. The analysis was carried out using a
Mindray BS-120 automated analyzer (Shenzhen Mindray Bio-Medical Electronics Co.,
Ltd) at Patholab Solutions Ghana Limited in Accra (Ghana). The reagents used in the
analysis were picric acid (26mmol/L), sodium hydroxide (1.6mmol/L), and
commercially prepared creatinine standard (176.8µmol/L).

4.6.6 Quality Control for Urinary Creatinine Analysis

As a quality control measure, duplicate sample for every 10\textsuperscript{th} sample was analysed to
determine the average Relative Percentage Difference (RPD) in creatinine
concentrations between samples and duplicates. A satisfactory RPD (±SD) of 2.5 ±
2.2% was obtained.

4.6.7 Calculation of Absorbed Daily Dose (ADD) from Urinary TCP

Estimation of chlorpyrifos ADD among applicators in the present study, for background
(LADD\textsubscript{B}) and post-application (ADD\textsubscript{A}) exposures followed the steps outlined below:
Step 1: Correcting TCP for Creatinine:

Daily urinary creatinine concentrations in µmol/L were converted to g/L by the equation:

\[
\text{Creatinine (g/L)} = \frac{\text{Creatinine (µmol/L)} \times \text{molecular weight of creatinine (113.12 g/mol)}}{1,000,000} \quad \text{Equation 4.4}
\]

To control for daily urine variation, the daily urinary TCP concentrations (µg/L) were then creatinine-normalized by expressing it as a ratio to the measured daily urinary creatinine (g/L), converting the units of TCP from µg/L to µg/g creatinine (Section 4.7.6). Thus,

\[
\text{TCP (µg/g creatinine)} = \frac{\text{TCP (µg /L urine)}}{\text{Creatinine (g/L urine)}} \quad \text{Equation 4.5}
\]

Step 2: Correcting Post-application TCP for Background TCP

There are multiple sources of TCP in the environment, such as from water and food (baseline or background exposure), in addition to occupational sources. Therefore, measured TCP levels in occupationally exposed individuals incorporates exposure from all pathways, which can lead to over-estimation of occupational exposure levels (Wilson et al., 2003; Lu et al., 2005; Barr and Angerer, 2006; Eaton et al., 2008). The quantities of TCP excreted for each of the post-application days were corrected for background TCP by subtracting the background/baseline TCP from the post-application TCP. The
corrected post-application TCPs were then summed to obtain total TCP excreted, which was attributable to a spray event.

**Step 3: Conversion of TCP to Absorbed Daily Dose (ADD)**

The applicators’ TCP levels were converted to ADD using the equation below (Farahat et al., 2010; Phung et al., 2013):

\[
\text{ADD (µg/kg/day)} = \frac{[C \times Cn \times CF \times (\text{MW}_{\text{CPF}}/\text{MW}_{\text{TCP}})]/\text{BW}}{\text{BW}} \quad \text{Equation 4.6}
\]

where, ADD is the Absorbed Daily Dose (µg/kg/day); C, the concentration of TCP excreted per day (µg/g); Cn, expected mass of creatinine excreted per day (g/day); CF, correction factor of 100/70 for urinary TCP (about 70% of chlorpyrifos is excreted as TCP in urine) (Nolan et al., 1984); MW_{CPF}, the molecular weight of chlorpyrifos (350.6g/mol); MW_{TCP} the molecular weight of TCP (198.5g/mol); and BW, the body weight of each applicator (kg).

Cn was calculated using the following formula (Mage et al., 2004):

\[
\text{Cn (g/day)} = \frac{[1.93(140-\text{Age (yrs.)}) \times \text{BW (kg)}^{1.5} \times \text{BH (cm)}^{0.5}]/1000, 000}{\text{BW}} \quad \text{Equation 4.7}
\]

where, BW is body weight; and BH, body height.
4.6.8 Calculation of Lifetime Average Daily Dose (LADD<sub>A</sub>)

Chronic exposure to chlorpyrifos due to occupational application (LADD<sub>A</sub>) among the applicators was estimated with the following equation (Phung et al., 2013):

\[
\text{LADD}_A = \frac{(\text{ADD} \times \text{EF} \times \text{ED})}{\text{AT}}
\]

Equation 4.8

where, ADD (µg/kg/day) is the Absorbed Daily Dose of chlorpyrifos of the applicator; EF, the Exposure Frequency (number of applications days per year); ED, the Exposure Duration (work lifetime years); and AT, the Averaging Time [(life expectancy in years – application start age in years) x 365 days/ year.

4.6.9 Data Analysis

General descriptive statistics determined to summarize the variables investigated were frequencies, proportions, means, standard deviations and ranges. Also, an evaluation was carried out to assess the relationships between ADD<sub>A</sub> (as a dependant variable) and field factors (as independent variables) which were observed and recorded during the application events. The ADD<sub>A</sub> data of the applicators were not normally distributed as judged by Shapiro-Wilk test (p < 0.001). Consequently, the non-parametric Spearman ρ test was applied to evaluate correlations between ADD<sub>A</sub> and continuous independent variables (application duration, insecticide formulation quantity, number of spray tanks, farm size, and crop height). For categorical independent variables (type of shirt, incidence of leaky tank, and incidence of insecticide spillage), the Mann-Whitney U test
was used to compare the differences in ADDA levels between groups. The SPSS computer program (Version 20) was used for the analysis.

4.7 Field Observation and Interview

The pesticide spraying activities of each applicator during the dermal sampling (Section 4.5.2) and urine sampling (Section 4.6.2) procedures were observed and documented by the research team. A guide (Appendix 4) was developed, in the form of a check-list, to facilitate the information collection during the field observations. The information collected included PPE usage, type of clothing worn, incidence of splash, spills, leakages, type of spraying equipment, duration of spraying, quantity of insecticide, crop height and farm size.

4.8 Dose-Response Assessment

4.8.1 Background

Conventionally, health risk assessment of exposure to toxicants are based on the use of guideline values, usually set using data from experimental studies on surrogate animals such as rats or mice. NOAEL and LOAEL from dose-response experimental data are divided by safety or uncertainty factors to give a guideline value. A guideline value is assumed to be a threshold value below which adverse effects would not be expected but above which occurrence of adverse effects can be expected. However, differences in sensitivities in a human population to a toxicant occur due to differences in factors such as age, sex and health status. It may therefore be difficult to establish an objective
threshold for the sensitivities of all members of a population (Daston, 1993; NRC, 2006).

An alternative approach is provided by the use of probabilistic techniques to express dose-response data in health risk assessment. These techniques offer the advantage that differing toxicant sensitivities within a population are taken into account. Nonetheless, experimental human dose-response data for toxicants are usually not available because such experiments with human populations under controlled conditions are not possible. Alternatively, Toxicant Sensitivity Distribution (TSD) data from human epidemiological studies may be used in human health risk assessment. With this novel technique, data from scientific literature reporting both toxicant adverse effects and the exposure levels are collated and expressed as cumulative probability distributions (Phung et al., 2015; Phung et al., 2017). Similar probabilistic techniques have been employed in the field of ecotoxicology to describe Species Sensitivity Distributions (SSD) of aquatic organisms from exposure to chlorpyrifos, atrazine, pentachlorophenol and cadmium (Solomon et al., 1996; McDaniel and Snell, 1999; Solomon et al., 2000).

Human TSD data have many deficiencies as well. For instance, the exposure dose and human population are not controlled. Also, there may be errors associated with sampling, exposure measurement, disease measurement and confounding factors (NRC, 2006). Nevertheless, the use of data from human epidemiological studies may offer a better option than surrogate animal data to assess health risks of human exposure to toxicants (Calderon, 2000; NRC, 2006). For instance, such data are directly applicable to human populations and therefore the guidelines obtained do not require
the application of safety factors to address uncertainties. Moreover, specific health effects can be ascertained at various exposure exceedances by comparison with the original TSD database.

4.8.2 Chlorpyrifos Adverse Response Dose from the Scientific Literature

A review of the scientific literature was carried out by Phung et al. (2015) to identify adverse effects of chlorpyrifos and the corresponding exposure levels from human epidemiological studies. When reported as urinary TCP, the exposure levels associated with adverse health effects were converted to chlorpyrifos as Absorbed Daily Dose (ADD) and Lifetime Absorbed Daily Dose (LADD) for acute and chronic effects, respectively. The following equations were respectively applied by Phung et al. (2013) and Phung et al. (2015) to convert urinary TCP measurements to chlorpyrifos:

\[
ADD (\mu g/kg/day) = [C \times Cn \times CF \times (MW_{CPF}/MW_{TCP})]/BW \quad \text{Equation 4.9}
\]

\[
LADD = (ADD \times EF \times ED)/AT \quad \text{Equation 4.10}
\]

where, ADD is the Absorbed Daily Dose of chlorpyrifos (\(\mu g/kg/day\)); C, the concentration of TCP excreted per day (\(\mu g/g\)); Cn, expected mass of creatinine excreted per day (g/day); CF, correction factor of 100/70 for urinary TCP (about 70% of chlorpyrifos is excreted as TCP in urine) (Nolan et al., 1984); \(MW_{CPF}\), the molecular weight of chlorpyrifos (350.6g/mol); \(MW_{TCP}\) the molecular weight of TCP.
(198.5g/mol); BW, the body weight of each applicator (kg); EF, the Exposure Frequency (number of applications days per year); ED, the Exposure Duration (work lifetime years); and AT, the Averaging Time (70 years × 365 days/year).

In the current study, the absorbed doses reported by Phung et al. (2015) were updated to include data from recent studies and analysed by similar procedures to Phung et al. (2015) (see Section 7.3 for details).

### 4.8.3 Data Analysis

Using Equation 4.4, the Cumulative Probabilities (CPs) of ADD and LADD values were calculated, after ranking the data points from the lowest to the highest. Cumulative Probability Distribution (CPD) plots of ADD and LADD were then constructed to obtain Toxicant Sensitivity Distribution (TSD) for acute (TSD\textsubscript{ACUTE}) and chronic (TSD\textsubscript{CHRONIC}) adverse effects of chlorpyrifos. The dose at the 5\textsuperscript{th} percentile (CP\textsubscript{5}) of each TSD was considered as the lowest dose above which the most sensitive group of the population may exhibit adverse effects (Connell, 2005). This dose was therefore identified as a Guideline Value (GV) for chlorpyrifos. Thus, the GV for chlorpyrifos chronic adverse effects was determined at CP\textsubscript{5} of TSD\textsubscript{CHRONIC}, and that for acute adverse effects was determined at CP\textsubscript{5} of TSD\textsubscript{ACUTE}. 

4.9 Health Risk Characterization Due to Chlorpyrifos Exposure with the Applicators

4.9.1 Background

Risk of adverse health effects among the applicators from exposure to chlorpyrifos was characterized by integrating the exposure data obtained (Section 4.5 and 4.6) with guideline values as well as the TSDs (Section 4.7.2) of chlorpyrifos. The adverse effects risk was initially evaluated using the Hazard Quotient (HQ) technique (Section 3.5) based on the exposure dose of the median-exposed (50th percentile) and the 5% highly exposed (95th percentile) groups. Subsequently, the proportion of adverse effects risk among all the applicators was evaluated using the Overall Risk Probability (ORP) and Monte-Carlo Simulation (MCS) techniques.

4.9.2 Data Analysis Using Hazard Quotient (HQ) Technique with Guideline Values (GV)

The estimated ADD and LADD of the applicators were used to construct CPD plots. The risk of adverse health effect was characterized as a ratio of the exposure dose at the 50th (HQ50) and 95th (HQ95) percentiles to a guideline value. Thus,

\[ HQ_{50} = \text{Exposure Dose at the 50th Percentile} / \text{Guideline Value} \quad \text{Equation 4.11} \]

\[ HQ_{95} = \text{Exposure Dose at the 95th Percentile} / \text{Guideline Value} \quad \text{Equation 4.12} \]
HQ values less or equal to unity are generally believed to be associated with a low probability for the occurrence of adverse health effects, whereas HQ values more than unity may be associated with high probability for the occurrence of adverse health effects.

4.9.3 Data Analysis Using Hazard Quotient (HQ) Technique with TSD Dose at CP5

In this research, a variant of the conventional HQ technique was also applied. With this variant, both the exposure dose and guideline value used to calculate HQ values were determined with probabilistic techniques (Section 3.5.2). HQ_{50/5} was calculated as the ratio of the exposure dose at the 50<sup>th</sup> percentile (CP<sub>50</sub>) (median exposed group) to the dose at the 5<sup>th</sup> percentile (CP<sub>5</sub>) of chlorpyrifos TSD dose obtained from human epidemiological studies (Section 7.3). HQ_{95/5} was similarly calculated from the exposure dose at the 95th percentile (CP<sub>95</sub>). Thus,

\[
HQ_{50/5} = \frac{\text{Exposure Dose at the 50<sup>th</sup> Percentile}}{\text{TSD Dose at CP5}} \quad \text{Equation 4.13}
\]

\[
HQ_{95/5} = \frac{\text{Exposure Dose at the 95<sup>th</sup> Percentile}}{\text{TSD Dose at CP5}} \quad \text{Equation 4.14}
\]

4.9.4 Data Analysis Using Overall Risk Probability (ORP) Technique

The ORP technique is a technique based on probabilistic distributions that is employed in health risk assessment to evaluate the level of risks pertaining to an exposure scenario utilising the distribution of both the exposure and the toxicant sensitivity. The technique is valuable in that it accounts for variabilities in both exposures and sensitivities to a
toxicant in the whole of a given population (Cao et al., 2011; Yu et al., 2011). With this technique, the CPD of both exposure and Toxicant Sensitivity Distribution (TSD) are plotted on the same graph. Using the CPD plot of the exposure, Exposure Exceedance values at any dose level are then calculated using the expression 100 – CP_{exposure}, where CP_{exposure} is any exposure cumulative probability. The corresponding percentages of the population exhibiting adverse effects (Affected Population) at these exposure exceedance values are evaluated from the CPD plot of the TSD. Hypothetical CPD plots of both Exposure and TSD doses are shown in Figure 4.7. The relationship of Exposure Exceedance and Affected Population is indicated which applies at any dose. The Exposure Exceedance values are subsequently plotted against the percentage of the Affected Population, to produce an Overall Risk Probability (ORP) curve (see Figure 4.8). The area under the curve is then calculated as the ORP value, which represents the proportion of the population who are at risk of adverse effects (Cao et al., 2011; Yu et al., 2011).
Figure 4.7: Hypothetical CPD Plot of Exposure Dose and TSD Dose Illustrating Relationships of Exposure Exceedance to Affected Population.

Figure 4.8: Hypothetical Plot of Exposure Exceedance Values and Corresponding Affected Population Derived from Figure 7.8.
4.9.5 Data Analysis Using Monte-Carlo Simulation (MCS) Technique

Monte-Carlo Simulation (MCS) is another technique based on probabilistic distributions that is employed to evaluate the risk of adverse effects in a population due to exposure to toxicants. The MCS technique utilizes the whole distribution of exposure and TSD to simulate the total proportion of a population that is at risk of adverse effects from a toxicant. Although the MCS technique is able to account for variability and uncertainty in risk characterization, factors involved in the technique itself may introduce some error in the final risk estimate. The stability of the risk estimate is dependent on the representativeness of the distribution type used for the input variables applied in the simulation model (Binkowitz and Wartenberg, 2001; Ferrier et al., 2006). The distribution types may be uniform, triangular, normal or lognormal. With environmental pollutants, exposure levels usually follow a lognormal distribution (Ott, 1990; Kon Kam King et al., 2015). Another factor that may introduce error with the MCS technique is the number of iterations used in the simulation process. To obtain a reliable risk estimate, the number of iterations should be sufficient. As a general rule, more iterations produce reliable estimates. However, too many iterations may be unnecessary and time consuming. Studies have shown that the optimum number of iterations for MCS can be between 5,000 to 10,000 (Mundfrom et al., 2011; Farrance and Frenkel, 2014).

In this study, the Monte Carlo Simulation model was built to calculate Hazard Quotient (HQ\textsubscript{MCS}) values as the ratios of exposure doses to toxicant sensitivity doses, using the means and standard deviations of the exposure doses and TSD doses. Based on a log-normal distribution for both the exposure and TSD doses, as judged by the Shapiro Wilk test (p > 0.05), the HQ\textsubscript{MCS} values were repeatedly and randomly calculated for 10,000
iterations. The simulations were performed using Oracle Crystal Ball® Monte Carlo software. The probability of \( HQ_{MCS} \) values exceeding unity constituted the proportion of the population at risk of adverse effects.
CHAPTER 5
HAZARD IDENTIFICATION WITH RICE FARMERS IN GHANA

5.1 Introduction

The conceptual framework of this research, based on the four-step health risk assessment framework of the United States’ National Research Council (USEPA, 2000; NRC, 2009), is shown in Figure 4.1 of Section 4.2 and repeated in this chapter as Figure 5.1. The figure illustrates how the chapters and sections of the research fit into the conceptual framework. The objectives of the overall research were to:

1. Identify hazardous pesticides and practices associated with the use of pesticides among applicators;
2. Assess the levels of chlorpyrifos exposure among applicators;
3. Evaluate the patterns of dermal exposure to chlorpyrifos among applicators;
4. Review the dose-response relationship of chlorpyrifos exposure and adverse effects;
5. Characterize the risks of adverse health effects due to chlorpyrifos exposure among applicators;

The objective of Chapter 5, highlighted with yellow colour in Figure 5.1, is to present the results and discussion on the hazard identification study (Section 4.4) carried out to address objective 1 of the overall research. Information provided in Chapter 5 includes the socio-demographic characteristics of the farmers; types of pesticide used; pesticide...
exposure risk factors; and the prevalence of self-reported pesticide poisoning symptoms among the farmers.

Figure 5.1: The Section on Hazard Identification
(Highlighted yellow in the overall research framework) (See Figure 4.1 in Section 4.2).
5.2 Socio-Demographic Characteristics of the Farmers

The socio-demographic characteristics of the farmers in this study are presented in Table 5.1. In all, 214 farmers across 22 villages participated in the study and 95% of the participants were male. This finding is not unexpected since the production of most cash crops in Ghana is carried out by men (Ntow et al., 2006; MoFA, 2009; Mattah et al., 2015) because they are usually the heads of families with a responsibility of providing financial support.

In terms of income, the farmers earned an average of GHS 3,200 (AUD 1,200) annually from rice production. With an average household size of about 4 persons (GSS, 2009), this amount may not be enough to adequately fund family expenses. Thus, most of the farmers may not be able to invest adequately in their farming activities, such as purchasing appropriate PPEs or hiring a trained pesticide applicator to apply pesticides.

The mean age of the farmers was 42 years with the majority (91%) of them aged below 56 years. A small proportion (9%) of the farmers belonged to the older group (above 55 years), who may be more vulnerable to pesticides health effects due to their age. For instance, damage to the nervous system of older people by chemical contamination is not easily repaired (Weiss, 2000). In addition, with 15 years of pesticide application on average, this group were likely to have experienced higher cumulative pesticide exposure.
Farming in Ghana is generally considered to be an occupation for less-educated and poor people. About 61% of the farmers studied were not educated beyond Junior High School level (nine years of formal education). With this low educational attainment, the farmers of this study risk not being able to read and understand pesticide labels properly.

Table 5.1: Socio-Demographic Characteristics of Rice Farmers in Ghana (n=214)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Number of Farmers Reporting</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
<td>204</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Age</td>
<td>25 years or less</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>26 to 35 years</td>
<td>54</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>36 to 45 years</td>
<td>69</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>46 to 55 years</td>
<td>60</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>56 years or more</td>
<td>20</td>
<td>9</td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>42 (±10.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Educational level attained</td>
<td>No formal education</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Primary</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Junior High</td>
<td>107</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Senior High and Vocational</td>
<td>69</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Tertiary</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>3,180 (±2,339)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annual farm income (GHS)</td>
<td>1,000 or less</td>
<td>29</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>1,001 - 2,000</td>
<td>38</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>2,001 - 3,000</td>
<td>48</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>3,001 - 4,000</td>
<td>32</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>4,001 or more</td>
<td>44</td>
<td>23</td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>3,180 (±2,339)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years of pesticide application by farmer</td>
<td>Up to 5</td>
<td>25</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>6 to 10</td>
<td>55</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>11 to 15</td>
<td>49</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>16 to 20</td>
<td>39</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>21 and above</td>
<td>46</td>
<td>22</td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>14.7 (±8.3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5.3 Pest Problems and Pesticides Use

The magnitude of the pest problems and usage of pesticides reported by the farmers are presented in Table 5.2. All farmers of the study revealed that insects (such as stem borers, termites, caterpillars and grasshoppers) and weeds (such as *Cyperus rotundus, Andropogon gayanus, Pennisetum spp., Cynodon dactylon, Panicum spp, Imperata cylindrica, and Chromolaena odorata*) were major pest problems on their farms. Fungal diseases (such as blast and smut) were also major problems for about 76% of the farmers. On average, the farmers estimated potential yield losses of about 51% if pesticides were not used. Consequently, all the farmers used pesticides as the main pest control strategy, with about 94% personally involved with mixing, loading and spraying. In a study conducted elsewhere in Ghana, Mattah *et al.* (2015) have similarly reported that about 92% of farmers who grow rice, maize, vegetables and fruits applied pesticides to treat diseases and pests. Likewise, studies conducted with vegetable farmers in Togo (Adjrah *et al*., 2013) and with rice farmers in Tanzania (Stadlinger *et al*., 2011) showed that about 98% and 82 to 84% of the farmers, respectively, used pesticides on their farms.

In Table 5.3 and Figure 5.2, the active ingredients and groups of pesticides used by the farmers are identified. Over 21 types of pesticide active ingredients were found to be used by the farmers. The most common group of pesticides used was weedicide (52%), followed by insecticides (28%) and fungicides (18%). Of the weedicides used, the main types were 2, 4-D, bispyribac-sodium and glyphosate, with usage prevalence of 51% for both 2, 4-D and bispyribac-sodium, and 48% for glyphosate. Whereas 2, 4-D is considered moderately hazardous to human health, bispyribac-sodium and glyphosate
are described as slightly hazardous (WHO, 2010). However, a recent study suggests that
glyphosate enhances the damaging effect of other environmental contaminants. In this
way, it could play a role in diseases and health conditions such as gastrointestinal
disorders, obesity, diabetes, heart disease, depression, autism, infertility, cancer and
Alzheimer’s disease (Samsel and Seneff, 2013).

With insecticides, the commonly used types were chlorpyrifos (83%) and lambda-
cyhalothrin (43%), both of which have been described by the WHO as moderately toxic
to humans (WHO, 2010). Exposure to chlorpyrifos has been associated with acute
health effects such as depression of cholinesterase activity, sub-clinical neuropathy and
memory problems, particularly with occupational exposure (Steenland et al., 2000;
Albers et al., 2007; Farahat et al., 2011). Also, chronic health effects such as fetal
neurodevelopment defects, altered thyroid functions and reductions in estradiol levels,
have been linked to chlorpyrifos exposure (Berkowitz et al., 2004; Meeker et al., 2006;
Meeker et al., 2008).

With the fungicides, sulfur was the dominant type, with a usage prevalence of 43%.
However, contrary to the situation observed with weedicides and insecticides, most of
the fungicides used by the farmers, including sulfur, were believed to be unlikely to
present an acute health hazard with normal use (WHO, 2010).

Generally, with the exception of the pyribenzoxim (obsolete pesticide) and carbofuran
(WHO toxicity Class Ib – highly hazardous), the rest of the pesticides used by the
farmers belong to WHO toxicity Classes II (moderately hazardous), III (slightly
hazardous), or Class U (unlikely to present acute hazard in normal use) (WHO, 2010), as reported in similar studies carried out in other parts of Ghana (Ntow et al., 2006; Mattah et al., 2015). The current regulations and programs in Ghana are aimed at reducing WHO hazard Class Ib (highly hazardous) pesticides and eliminating WHO Class Ia (extremely hazardous) pesticides (EPAG, 2016).

Table 5.2: Pest Problems and Pesticides Use on Rice Farms in Ghana (n = 214)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Number of Farmers Reporting (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have problems with insects</td>
<td>Yes</td>
<td>214 (100)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0(0)</td>
</tr>
<tr>
<td>Have problems with weeds</td>
<td>Yes</td>
<td>214(100)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0(0)</td>
</tr>
<tr>
<td>Have problems with fungus</td>
<td>Yes</td>
<td>161(76)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>52(24)</td>
</tr>
<tr>
<td>Self-estimated potential yield loss from pest attack (%)</td>
<td>0 to 20(%)</td>
<td>13(7)</td>
</tr>
<tr>
<td></td>
<td>21 to 40(%)</td>
<td>57(29)</td>
</tr>
<tr>
<td></td>
<td>41 to 60(%)</td>
<td>88(44)</td>
</tr>
<tr>
<td></td>
<td>61 to 80(%)</td>
<td>29(15)</td>
</tr>
<tr>
<td></td>
<td>81 to 100(%)</td>
<td>12(6)</td>
</tr>
<tr>
<td></td>
<td>Mean (±SD) = 51.4±19.2</td>
<td></td>
</tr>
<tr>
<td>Farmer use pesticides on the farm</td>
<td>Yes</td>
<td>214(100)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0(0)</td>
</tr>
<tr>
<td>Farmer mixes, loads, and applies pesticides</td>
<td>Yes</td>
<td>202(94)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>12(6)</td>
</tr>
</tbody>
</table>
Table 5.3: Types of Pesticide Active Ingredient Used by Rice Farmers in Ghana (n=214)

<table>
<thead>
<tr>
<th>Pesticide Group</th>
<th>Active Ingredient</th>
<th>Number of Farmers Reporting (%)</th>
<th>Pesticide Chemical Class</th>
<th>WHO Toxicity Class (WHO, 2010)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weedicides</td>
<td>Pyribenzoxim</td>
<td>24 (11)</td>
<td>Unclassified</td>
<td>Obsolete</td>
</tr>
<tr>
<td></td>
<td>Pendimethalin</td>
<td>17 (8)</td>
<td>Dinitroaniline</td>
<td>Moderately hazardous</td>
</tr>
<tr>
<td></td>
<td>Prapanil</td>
<td>82 (38)</td>
<td>Anilide</td>
<td>Moderately hazardous</td>
</tr>
<tr>
<td></td>
<td>2,4-D</td>
<td>109 (51)</td>
<td>Phenoxyacetic acid</td>
<td>Moderately hazardous</td>
</tr>
<tr>
<td></td>
<td>Paraquat</td>
<td>2 (1)</td>
<td>Bipyridylium</td>
<td>Moderately hazardous</td>
</tr>
<tr>
<td></td>
<td>Glyphosate</td>
<td>103 (48)</td>
<td>Phosphonoglycine</td>
<td>Slightly hazardous</td>
</tr>
<tr>
<td></td>
<td>Bispyribac-sodium</td>
<td>108 (51)</td>
<td>Pyrimidinloxybenzoic acid</td>
<td>Slightly hazardous</td>
</tr>
<tr>
<td></td>
<td>Bensulfuron-methyl</td>
<td>41 (19)</td>
<td>Pyrimidinylsulfonyleurea</td>
<td>Unlikely to present acute hazard in normal use</td>
</tr>
<tr>
<td></td>
<td>Pretilachlor</td>
<td>24 (11)</td>
<td>Chloroacetanilide</td>
<td>Unlikely to present acute hazard in normal use</td>
</tr>
<tr>
<td>Insecticides</td>
<td>Carbofuran</td>
<td>12 (6)</td>
<td>Carbamate</td>
<td>Highly hazardous</td>
</tr>
<tr>
<td></td>
<td>Lambda-cyhalothrin</td>
<td>91 (43)</td>
<td>Pyrethroid</td>
<td>Moderately hazardous</td>
</tr>
<tr>
<td></td>
<td>Acetamiprid</td>
<td>1 (1)</td>
<td>Neonicotinoid</td>
<td>Moderately hazardous</td>
</tr>
<tr>
<td></td>
<td>Chloropyrifos</td>
<td>178 (83)</td>
<td>Organophosphosphate</td>
<td>Moderately hazardous</td>
</tr>
<tr>
<td>Fungicides</td>
<td>Tebuconazole</td>
<td>24 (11)</td>
<td>Triazole</td>
<td>Moderately hazardous</td>
</tr>
<tr>
<td></td>
<td>Difenoconazole</td>
<td>10 (5)</td>
<td>Triazole</td>
<td>Moderately hazardous</td>
</tr>
<tr>
<td></td>
<td>Copper Hydroxide</td>
<td>1 (1)</td>
<td>Inorganic</td>
<td>Moderately hazardous</td>
</tr>
<tr>
<td></td>
<td>Sulfur</td>
<td>91 (43)</td>
<td>Inorganic</td>
<td>Unlikely to present acute hazard in normal use</td>
</tr>
<tr>
<td></td>
<td>Azoxyystrobin</td>
<td>10 (5)</td>
<td>Strobilurin</td>
<td>Unlikely to present acute hazard in normal use</td>
</tr>
<tr>
<td></td>
<td>Trifloxystrobin</td>
<td>24 (11)</td>
<td>Strobilurin</td>
<td>Unlikely to present acute hazard in normal use</td>
</tr>
<tr>
<td></td>
<td>Maneb</td>
<td>4 (2)</td>
<td>Carbamate</td>
<td>Unlikely to present acute hazard in normal use</td>
</tr>
<tr>
<td></td>
<td>Mancozeb</td>
<td>16 (8)</td>
<td>Carbamate</td>
<td>Unlikely to present acute hazard in normal use</td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td>18 (8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 5.2 Common Groups of Pesticides Used by Rice Farmers in Ghana
5.4 Pesticide Exposure Risk Factors

Some factors that may potentially increase the risk of pesticide exposure among the farmers are shown in Table 5.4. About 40% have no training on pesticide safety. Also, about 15% do not read and/or understand the labels on the pesticides they apply. There are therefore reasonable grounds to suggest that many of the farmers in this study have limited knowledge regarding the potential health effects and appropriate use of pesticides. In a related study conducted in Ethiopia, Mekonnen and Agonafir (2002) reported that 67% of the farmers did not understand the information on the pesticide they applied. Inadequate pesticide knowledge may be associated with hazardous pesticide handling practices (Salameh et al., 2004) which may in turn lead to high exposure (Krenz et al., 2015).

Reflecting the inadequate pesticide safety training reported by some of the farmers in this study, unsafe pesticide handling practices were reported as well. For instance, about 90% of the farmers accidentally spill significant quantities of pesticides during mixing, loading, or spraying. Compounding these practices is limited use of PPEs. Only about 22% used PPEs during mixing, loading, or spraying of pesticides, as similarly reported elsewhere (Del Prado-Lu, 2007; Williamson et al., 2008; Stadlinger et al., 2011; Adjrah et al., 2013; Mattah et al., 2015). However, the type of PPE used by the farmers consisted of only googles to protect the eye. Therefore, most part of the body of the farmers would not be adequately protected.

With the applicators of the present study, a major factor preventing the use of protective boots while spraying pesticides is the presence of thick mud on the irrigated fields that
make it almost impossible to walk when they wear the boots. They therefore prefer to walk bare-footed while spraying pesticides (information obtained through interaction with some of the farmers and Agricultural Extension Agents). In addition, the hot and humid weather conditions in these areas, make it uncomfortable for farmers to use PPEs (Clarke et al., 1997; Mekonnen and Agonafir, 2002; Issa et al., 2010; Adjrah et al., 2013). Also, reasons such as unavailability of PPE for purchase, financial challenges and belief that pesticides are not harmful, contribute to less use of PPEs (Clarke et al., 1997; Issa et al., 2010; Stadlinger et al., 2011).

Most of the farmers protected themselves by wearing long pants and long-sleeved shirts when mixing, loading and spraying of pesticides. This may provide some form of protection against pesticide exposure as suggested by Phung et al. (2012a). However, this may not be sufficient to prevent exposure, especially with long spraying durations, which usually allows more time for pesticides to penetrate most ordinary farm clothing to reach the skin of applicators. Inert components of pesticide formulations, meant to enhance penetration and retention on plant leaves, could have similar effects on garments made from natural fibres such as cotton (Laughlin et al., 1985; Cox and Surgan, 2006). Also, applicators usually sweat excessively in hot weather conditions, which could enhance the absorption of pesticides (Williams et al., 2004).

Hand operated knapsack sprayers were the only means (100%) by which pesticides were applied by the farmers in this study (Table 5.4). Spraying pesticides with knapsack sprayers may lead to high exposure (Lozier et al., 2013). This may be because of frequent incidences of pesticide spillages, leaky spraying tanks or nozzles, applicators
touching the nozzles of the spray device with bare hands, and non-calibration of spraying equipment (Mureithi et al., 2011; Lekei et al., 2014).

Table 5.4: Pesticide Exposure Risk Factors among Rice Farmers in Ghana (n = 214)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Category</th>
<th>Number of Farmers Reporting (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have received training on pesticide safety</td>
<td>Yes</td>
<td>125 (60)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>82 (40)</td>
</tr>
<tr>
<td>Read and understand pesticide label before using</td>
<td>Yes</td>
<td>176 (85)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>31 (15)</td>
</tr>
<tr>
<td>Re-entry time after spraying</td>
<td>1 day or less</td>
<td>89 (43)</td>
</tr>
<tr>
<td></td>
<td>2 to 3 days</td>
<td>61 (29)</td>
</tr>
<tr>
<td></td>
<td>More than 3 days</td>
<td>59 (28)</td>
</tr>
<tr>
<td>Suck or blow nozzle of spraying equipment with the mouth when blocked</td>
<td>Yes</td>
<td>67 (34)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>129 (66)</td>
</tr>
<tr>
<td>Accidentally spills pesticides when mixing, loading or spraying pesticides</td>
<td>Yes</td>
<td>179 (90)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>20 (10)</td>
</tr>
<tr>
<td>Showers immediately after spraying</td>
<td>Yes</td>
<td>196 (97)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Drink, eat or chew anything during pesticide mixing, loading or application</td>
<td>Yes</td>
<td>66 (33)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>137 (67)</td>
</tr>
<tr>
<td>Use PPE (s) during pesticide application</td>
<td>Yes</td>
<td>44 (22)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>159 (78)</td>
</tr>
<tr>
<td>Type of spray device used</td>
<td>Knapsack</td>
<td>214 (100)</td>
</tr>
</tbody>
</table>

5.5 Self-reported Acute Pesticide Poisoning Symptoms

The Intergovernmental Forum on Chemical Safety (IFCS), hosted by the WHO, defines Acute Pesticide Poisoning (APP) as any medical condition due to suspected or confirmed exposure to pesticide within 48 hours (Thundiyil, 2008). Such medical conditions are usually associated with the gastrointestinal, respiratory, nervous, cardiovascular, metabolic, renal, muscular, dermatologic, and ocular organs of the human body. Specifically, the symptoms may include vomiting, chest pains, blurred
vision, hypertension, acidosis, polyuria, muscle pain, skin irritation and ocular burns (Thundiyil, 2008).

Figure 5.3 shows the prevalence of some self-reported acute poisoning symptoms of pesticides as listed by the IFCS (Thundiyil, 2008). All the farmers who sprayed pesticides had experienced symptoms compatible with acute poisoning. The most prevalent of the symptoms were excessive tiredness (93%) blurred vision (70%), skin rashes (69%), headache (59%) dizziness (57%), and sleeping difficulty (56%). Although the symptoms reported are non-specific, the period within which they were experienced by the farmers is at least suggestive that the symptoms could be associated with pesticide spraying activities. Figure 5.4 shows the periods after spraying within which the symptoms were experienced by the farmers. About 91% of the symptoms were experienced within 24 hours after spraying, which is well within the 48-hour post-exposure period proposed by the IFCS (Thundiyil, 2008). Nevertheless, biological or environmental monitoring with the farmers could provide stronger evidence of pesticide exposure (Mancini et al., 2005; Thundiyil, 2008). Also, the outcomes of such monitoring activities could be used to characterize the levels of health risks associated with the exposure, as done with chlorpyrifos (Phung et al., 2013) and other environmental contaminants (Hamidin et al., 2013; Edokpolo et al., 2015).

About 53% of the farmers indicated that they sought medical attention for the symptoms they experienced by attending a health centre or consulting pharmacists. This attendance rate is higher compared to similar studies conducted in Tanzania (34%), Zimbabwe (3-7%) and Côte d'Ivoire (1.5-2.4%) (Maumbe and Swinton, 2003; Ajayi et al., 2011;
Lekei et al., 2014). The differences in the attendance rates could be attributed to differences in the definition given to the outcome measure. In this study and that conducted in Tanzania (Lekei et al., 2014), the outcome measure included attendance to health centres and pharmacy shops. However, the measure in the studies conducted in Zimbabwe (Maumbe and Swinton, 2003) and Côte d’Ivoire (Ajayi et al., 2011) accounted for only attendance to health centres.

Many farmers in less developed countries who experience pesticide poisoning usually fail to seek medical attention from health centres. Very often, the farmers get accustomed to the symptoms and thereby under-estimate the severity as well as the need to seek medical attention (Ajayi et al., 2011). In addition, poverty, poor roads, and long distance to health centres may also contribute to this situation (Halwindi et al., 2013; Schwitters et al., 2015). The situation denies health centres the opportunity to record pesticide poisoning incidences. Without such records, it is difficult for the relevant institutions to develop policies and programs to address the issue (Rother, 2014).
Figure 5.3 Self-Reported Symptoms of Pesticide Poisoning Experienced After Spraying by Rice Farmers in Ghana.

Figure 5.4: Period within Which Pesticide Poisoning Symptoms Were Experienced After Spraying by Rice Farmers in Ghana.
5.6 Summary

The hazard identification study has shown that there was widespread use of pesticides among the farmers, in contrast to the Integrated Pest Management (IPM) policy of the Ministry of Food and Agriculture. The most common pesticide active ingredient applied by the farmers was chlorpyrifos (used by 83% of the farmers), a moderately toxic insecticide. Others were 2, 4-D, bispyribac-sodium, glyphosate, lambda-cyhalothrin and sulfur, with usage prevalence of 51%, 51%, 48%, 43% and 43%, respectively.

Some characteristics identified that may predispose the farmers to excessive exposure include low educational attainment (61%), no training on pesticide safety (40%), frequent spillage of pesticides during use (90%), and no use of PPEs (78%).
All the farmers that applied pesticides experienced symptoms that were compatible with known symptoms of pesticide poisoning. Close to half (47%) of the farmers did not seek medical attention for the symptoms they experienced.
6.1 Dermal Chlorpyrifos Exposure with the Applicators

6.1.1 Introduction

The conceptual framework of this research, based on the four-step health risk assessment framework of the United States’ National Research Council (USEPA, 2000; NRC, 2009), is shown in Figure 4.1 of Section 4.2 and repeated in this section as Figure 6.1. The figure illustrates how the chapters and sections of the research fit into the conceptual framework. The objectives of the overall research were to:

1. Identify hazardous pesticides and practices associated with the use of pesticides among applicators;
2. Assess the levels of chlorpyrifos exposure among applicators;
3. Evaluate the patterns of dermal exposure to chlorpyrifos among applicators;
4. Review the dose-response relationship of chlorpyrifos exposure and adverse effects;
5. Characterize the risks of adverse health effects due to chlorpyrifos exposure among applicators;
The initial hazard identification study (Chapter 5) with the farmers indicated that chlorpyrifos was a potential health problem. About 83% of the farmers applied chlorpyrifos on their farms. Chlorpyrifos is moderately toxic to humans (WHO, 2010). All the farmers who applied pesticides complained of symptoms that were compatible with known acute poisoning symptoms (Thundiyil, 2008) (Figure 5.3).

The objective of Section 6.1, highlighted blue in Figure 6.1, is to present the results and discussion of the study (Section 4.5) conducted to evaluate dermal exposure to chlorpyrifos among the rice farmers using the whole-body dermal dosimetry method. Section 6.1 addressed objectives 2 and 3 of the overall research. The information obtained from this dermal evaluation will be used in Section 8.1 of the research to characterize risk of adverse health effects with the applicators.
Figure 6.1: The Section on Chlorpyrifos Exposure Estimated from Whole-Body Dermal Dosimetry (highlighted blue in the overall research framework) (see Figure 4.1 in Section 4.2)
6.1.2 Personal Characteristics of the Applicators and Observed Field Factors during Application

All the applicators were male aged between 23 to 53 years (mean, 40 years). Fifty eight percent of the applicators were educated up to Junior High School (JHS) level, whereas the rest (42%) had education above this level. The applicators had used insecticides for between 5 and 32 years with a mean of 16 years.

The observed field factors during application are outlined in Table 6.1. Most the applicators (54%) had received training on pesticide safety from Ghana’s Ministry of Food and Agriculture and/ or non-governmental organisations through seminars. Short sleeve shirts with long trousers made with cotton were the predominant form of apparel (58%). Only one applicator (4%) used any form of PPE. This consisted of safety glasses to protect the eyes. Incidences of pesticide leakage and spillage were recorded among 63% and 83% of the applicators, respectively. The farm size and the height of crops sprayed ranged from 0.2 to 1.0 ha (mean, 0.5 ha) and 10 to 85 cm (mean, 42 cm), respectively. The duration and insecticide quantity during one spray event ranged from 21 to 110 minutes (mean, 57 minutes) and 100 to 325 mL (mean, 182 mL), respectively.
Table 6.1: Observed Field Factors During Spraying of Rice Crops with Chlorpyrifos by Applicators in Ghana (n = 24)

<table>
<thead>
<tr>
<th>Applicator ID</th>
<th>Trained on pesticide safety</th>
<th>Type of Shirt*</th>
<th>Type of PPE</th>
<th>Leaky tank</th>
<th>Spillage</th>
<th>Farm size (ha)</th>
<th>Crop height (cm)</th>
<th>Quantity of Insecticide Applied (mL)</th>
<th>Spraying Duration (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 / A**</td>
<td>Yes</td>
<td>Short sleeved</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>1.0</td>
<td>80</td>
<td>275</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>Yes</td>
<td>Long sleeved</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>0.2</td>
<td>65</td>
<td>100</td>
<td>24</td>
</tr>
<tr>
<td>3 / B**</td>
<td>Yes</td>
<td>Short sleeved</td>
<td>None</td>
<td>Yes</td>
<td>No</td>
<td>0.9</td>
<td>50</td>
<td>300</td>
<td>83</td>
</tr>
<tr>
<td>4</td>
<td>No</td>
<td>Short sleeved</td>
<td>None</td>
<td>No</td>
<td>No</td>
<td>0.3</td>
<td>16</td>
<td>100</td>
<td>21</td>
</tr>
<tr>
<td>5</td>
<td>No</td>
<td>Short sleeved</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>0.5</td>
<td>20</td>
<td>150</td>
<td>47</td>
</tr>
<tr>
<td>6</td>
<td>Yes</td>
<td>Short sleeved</td>
<td>None</td>
<td>Yes</td>
<td>No</td>
<td>0.9</td>
<td>50</td>
<td>300</td>
<td>110</td>
</tr>
<tr>
<td>7</td>
<td>Yes</td>
<td>Short sleeved</td>
<td>None</td>
<td>No</td>
<td>No</td>
<td>0.6</td>
<td>15</td>
<td>150</td>
<td>50</td>
</tr>
<tr>
<td>8</td>
<td>Yes</td>
<td>Long sleeved</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>0.3</td>
<td>60</td>
<td>200</td>
<td>27</td>
</tr>
<tr>
<td>9 / C**</td>
<td>Yes</td>
<td>Long sleeved</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>0.4</td>
<td>12</td>
<td>125</td>
<td>44</td>
</tr>
<tr>
<td>10 / D**</td>
<td>No</td>
<td>Short sleeved</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>0.9</td>
<td>30</td>
<td>275</td>
<td>82</td>
</tr>
<tr>
<td>11</td>
<td>Yes</td>
<td>Short sleeved</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>0.5</td>
<td>40</td>
<td>150</td>
<td>48</td>
</tr>
<tr>
<td>12</td>
<td>Yes</td>
<td>Long sleeved</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>0.2</td>
<td>55</td>
<td>200</td>
<td>21</td>
</tr>
<tr>
<td>13</td>
<td>No</td>
<td>Long sleeved</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>0.2</td>
<td>35</td>
<td>100</td>
<td>21</td>
</tr>
<tr>
<td>14</td>
<td>Yes</td>
<td>Long sleeved</td>
<td>Safety glasses</td>
<td>No</td>
<td>No</td>
<td>0.5</td>
<td>60</td>
<td>150</td>
<td>55</td>
</tr>
<tr>
<td>15</td>
<td>No</td>
<td>Short sleeved</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>0.8</td>
<td>65</td>
<td>325</td>
<td>94</td>
</tr>
<tr>
<td>16</td>
<td>No</td>
<td>Short sleeved</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>0.3</td>
<td>30</td>
<td>150</td>
<td>45</td>
</tr>
<tr>
<td>17</td>
<td>No</td>
<td>Short sleeved</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>0.8</td>
<td>65</td>
<td>150</td>
<td>75</td>
</tr>
<tr>
<td>18</td>
<td>No</td>
<td>Short sleeved</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>0.4</td>
<td>10</td>
<td>100</td>
<td>69</td>
</tr>
<tr>
<td>19</td>
<td>No</td>
<td>Short sleeved</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>0.3</td>
<td>85</td>
<td>200</td>
<td>36</td>
</tr>
<tr>
<td>20</td>
<td>Yes</td>
<td>Long sleeved</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>0.4</td>
<td>45</td>
<td>150</td>
<td>47</td>
</tr>
<tr>
<td>21</td>
<td>No</td>
<td>Long sleeved</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>0.4</td>
<td>45</td>
<td>150</td>
<td>44</td>
</tr>
<tr>
<td>22</td>
<td>Yes</td>
<td>Long sleeved</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>0.4</td>
<td>35</td>
<td>200</td>
<td>51</td>
</tr>
<tr>
<td>23</td>
<td>No</td>
<td>Short sleeved</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>0.4</td>
<td>20</td>
<td>163</td>
<td>69</td>
</tr>
<tr>
<td>24</td>
<td>Yes</td>
<td>Long sleeved</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>0.8</td>
<td>30</td>
<td>200</td>
<td>110</td>
</tr>
</tbody>
</table>

Summary:  
- Yes (54%), No (46%)  
- Long sleeved (42%), Short sleeved (58%)  
- Used PPE (4%), No PPE (96%)  
- Yes (63%), No (37%)  
- Yes (83%), No (17%)  
- Mean (0.5) S.D (0.25) S.E.M (0.05)  
- Mean (42) S.D (22) S.E.M (4.4)  
- Mean (182) S.D (68) S.E.M (13.8)  
- Mean (57) S.D (27) S.E.M (5.5)

* All of the applicators wore long pants.

** A, B, C, and D - The four applicators whose body suits were analysed separately according to the body sections shown in Figure 4.5 with dermal exposure in Table 6.2.
6.1.3 Total Dermal Exposure (TDE) and Unit Exposure (UE)

The Cumulative Probability Distribution (CPD) plots of TDE and UE values of chlorpyrifos found with the applicators studied are provided in Figures 6.2 and 6.3, respectively. The linear part of the CPD plots of environmental pollutant levels is usually determined to lie between 20% or below (lower bound) and 80% or above (upper bound) of the CPD (Edokpolo et al., 2015; Sadler et al., 2016). In this study, the linear part of the CPD for TDE and UE were determined to be between 4% - 96% and 12% - 88% of the CPD, respectively, based on the coefficient of determination ($R^2$) values. The corresponding regression equation for the linear part of the CPD plots, respectively were:

$$\text{CP (\%)} = 150\log\text{TDE} - 156 \quad (R^2 = 0.94, \ p < 0.0001) \quad \text{Equation 6.1}$$

$$\text{CP (\%)} = 189\log\text{UE} + 340 \quad (R^2 = 0.99, \ p < 0.0001) \quad \text{Equation 6.2}$$

Figure 6.2 shows that, for a day’s spray event, TDE at the 50th percentile cumulative probability ($CP_{50}$) was 24 mg, while TDE at the 95th percentile cumulative probability ($CP_{95}$) was 48 mg. Likewise, Figure 6.3 indicates that the UE value at $CP_{50}$ and $CP_{95}$ were 0.03% and 0.06%, respectively. $CP_{50}$ is the level of exposure among the median-exposed group, whereas $CP_{95}$ is the level of exposure among the 5% most highly-exposed group.
The UE values (0.01 – 0.06%) from the present study is similar to reported UE values (Choi et al., 2013; Moon et al., 2013) ranging from 0.01 – 0.04% and 0.01 - 0.05%, respectively, during the application stage. Choi et al. (2013) evaluated the UE values from imidacloprid exposure among applicators who sprayed green pepper, cucumber, rice and apple crops, while Moon et al. (2013) evaluated fenvalarate exposure among applicators who sprayed apple crops. However, during the mixing and loading stage, both Choi et al. (2013) and Moon et al. (2013) reported lower UE values (0.001 to 0.008% and 0.001 to 0.002%, respectively). This implies that the exposure levels during the mixing and loading stage were less than those during the application stage. It is noteworthy that, unlike the studies conducted by Choi et al. (2013) and Moon et al.(2013), the UE values obtained in the present study were for both mixing/loading and spraying stages.

Figure 6.2: Cumulative Probability Distribution Plot of Total Dermal Exposure of Chlorpyrifos with Applicators on Rice Farms in Ghana.
In contrast to the findings of the present study, a relatively higher UE value (0.10%) has been reported by An et al. (2015) in a study conducted among applicators who sprayed cucumbers in greenhouses with chlorpyrifos and chlorothalonil. The differences in the UE values between the study by An et al. (2015) and the present study could be due to the different types of knapsack sprayers used by the applicators in the two studies. Whereas hand-pressurized knapsack sprayers were used by applicators in the present study, the applicators in the study by An et al. (2015) used powered knapsack sprayers. Powered knapsack sprayers usually produce higher spray pressure and could therefore lead to higher levels of exposure on applicators.
Information on UE values of pesticides in different handling scenarios from the USA and Canadian pesticide field conditions have been used by the United States Environmental Protection Agency (USEPA) and Health Canada to develop a Pesticide Handlers Exposure Database (PHED) (Nielsen et al., 1995). The database has two main assumptions: (1) exposure is proportional to the quantity of AI applied; and (2) exposure dose depends mainly on the method of application and the formulation type, but not the physico-chemical properties of the AI applied (Sielken Jr, 2005; Beauvais et al., 2007). However, the second assumption regarding physico-chemical properties is only valid for AIs with vapour pressures below $7.5 \times 10^{-4}$ mmHg ($1\times10^{-4}$kPa) for outdoor use at 20 to 30°C (Norman, 2005). These include chlorpyrifos, which has a vapour pressure of $1.0 \times 10^{-3}$ Pa at 25°C (WHO, 2009c). Using the PHED and more recent databases such as the Agricultural Handlers Exposure Database (AHED), the USEPA has created an Occupational Pesticide Handler Unit Exposure Surrogate Reference Table (OPHUESRT) (USEPA, 2016). With appropriate absorption factors, this unit exposure information can be used to estimate pesticide exposure for a use scenario, when actual exposure data are not available.

The UE value (0.03%) obtained in the present study among the median exposed group ($C_{P50}$) of the applicators was thrice the dermal UE value of 0.01% (when converted to metric mass units from the stated 58,400μg /pound AI) for a similar pesticide use scenario of the USEPA’s unit exposure surrogate reference table (USEPA, 2016). The UE value (0.06%) found among the 5% highly exposed group of the present study was six times higher than the USEPA’s UE value stated above. These results suggest that applicators of the present study were at risk of excessive levels of exposure compared to applicators in North American countries. In addition, the applicators had used pesticides
for about 16 years with consequent repeated high exposure. The high UE values obtained in the present study, compared to that of the USEPA’s unit exposure surrogate reference table, OPHUESRT, could be due to differences in the safety practices between pesticide applicators of North American countries and applicators in the present study.

6.1.4 Patterns of Pesticide Exposure

Patterns on Individual Anatomical Regions of the Applicators

The patterns of chlorpyrifos exposure on the anatomical regions was evaluated with four randomly selected applicators (Table 6.1, A, B, C and D) from the study group as presented in Table 6.2. Some differences were observed regarding the patterns of chlorpyrifos depositon at the level of individual applicators. These differences probably reflected the field factors reported in Table 6.1. Applicators A, C, and D had the highest proportion of exposure on the hands (28 %, 88 %, and 23 % of TDE, respectively), compared to applicator B whose hand exposure was 16 % of TDE. This might be due to spillage that was observed during mixing and loading of pesticides by applicators A, C, and D, but not with applicator B. Also, Table 6.1 shows that the height of the crops sprayed by applicators A and B (80 cm and 50 cm, respectively), were greater than those of the crops sprayed by applicators C and D (12 cm and 30 cm, respectively). Consequently, the proportions of exposure on the upper legs of applicators A and B (28% and 21%, respectively) were higher than those of applicators C and D (0.4% and 14%, respectively) since taller crops may allow contaminated leaves to reach the upper legs of applicators. In addition, the applicator who wore a long sleeve shirt (applicator C) had a relatively lower proportion of exposure (0.1%) on the lower arms than applicators A, B and D (about 2% and 1%, and 12%, respectively), who wore short
sleeve shirts. Moreover, incidence of spray tank leakage affected the proportion of exposure at the back abdomen of the applicators. The applicators whose spray tank leaked (applicators B and D), had the highest proportion of exposure (19% and 13%, respectively) at the back abdomen, compared to applicators A (0.5%) and C (0.7%). Interestingly, applicators B and D also had the highest proportion of exposure on the front abdomen (16% and 11%, respectively), compared to applicators A (2%) and C (0.3%). The reason for this finding is not immediately clear but may suggest that leaked insecticide may have reached the front abdomen.

Table 6.2: Pattern of Chlorpyrifos Deposition on the Anatomical Regions of Individual Applicators on Rice Farms in Ghana.

<table>
<thead>
<tr>
<th>Body Section*</th>
<th>Proportion of Total Dermal Exposure (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Applicator A**</td>
</tr>
<tr>
<td>Head</td>
<td>1</td>
</tr>
<tr>
<td>Front abdomen</td>
<td>2</td>
</tr>
<tr>
<td>Back abdomen</td>
<td>0.5</td>
</tr>
<tr>
<td>Upper arm</td>
<td>0.2</td>
</tr>
<tr>
<td>Lower arm</td>
<td>2</td>
</tr>
<tr>
<td>Hands</td>
<td>28</td>
</tr>
<tr>
<td>Upper legs</td>
<td>28</td>
</tr>
<tr>
<td>Lower legs</td>
<td>28</td>
</tr>
<tr>
<td>Feet</td>
<td>11</td>
</tr>
</tbody>
</table>

*see Figure 4.5
**see Table 6.1 for the observed field factors with these applicators

The general pattern of chlorpyrifos deposition on the anatomical regions, evaluated with the four applicators, is presented in Figure 6.4. Overall, the anatomical region that received the highest proportion of exposure with the applicators studied was the hands. Contamination on the hands constituted about 39% of TDE. The next highly exposed anatomical regions were the lower legs (17%), upper legs (16%), back abdomen (8%),
The least exposed anatomical regions were the lower arms (4%), head (2%), and the upper arms (1%).

Except for the feet and the lower arms, the chlorpyrifos skin loading of the anatomical regions of the applicators followed a similar pattern to that of the general proportion of exposure described above. The hands were the primary site of contamination in terms of chlorpyrifos skin loading (13 µg/cm²). The feet (3 µg/cm²), lower legs (3 µg/cm²), upper legs (3 µg/cm²) and lower arms (1 µg/cm²) were secondary sites of exposure, with the lowest levels of exposure being found on the back abdomen (0.9 µg/cm²), front abdomen (0.8 µg/cm²), head (0.3 µg/cm²) and upper arms (0.3 µg/cm²). None of the
applicators used any form of hand gloves, which might have contributed to the relatively high level of exposure of the hands found with applicators in the present study. Activities during the mixing and loading stages with the applicators in the present study involved the use of the hands. Also, the hands were used to adjust and clear the nozzle of the spray device.

A similar study conducted among applicators who sprayed malathion on greenhouse tomato plants revealed that contamination on the hands was about 76% of the total dermal exposure (Machera, 2003). Likewise, hand contamination represented between 85% - 99% of total dermal exposure among agricultural subcontractors who did not use hand gloves (Vitali et al., 2009). Also, among applicators in vineyards, hand contamination was the highest and accounted for 49% and 56% of total dermal exposure during mixing and spraying stages, respectively (Baldi et al., 2006). Evaluation of exposure to acetamiprid with applicators in a greenhouse watermelon farm revealed that the highest level of contamination was on the hands during mixing and loading of pesticides into the spray tank (Kim et al., 2014). Related outcomes have also been found with applicators who used chlorpyrifos on maize crops (Gao et al., 2014); procymidone and deltamethrin on greenhouses tomato crops (Ramos et al., 2010); and fenvalarate on apple crops (Moon et al., 2013). Compared to the left hand, the right hand which usually held the spray lance, was the most contaminated (An et al., 2014; Gao et al., 2014).

However, hand contamination was less prominent in another study (Cao et al., 2015). This study evaluated exposure of imdacloprid to applicators who sprayed wheat crops
using knapsack sprayers. The upper and lower legs contributed the most (76% to 88%) to total exposure. The legs were also identified as the site of highest exposure (48% of total exposure) in a study conducted among applicators who sprayed rose plants in greenhouse with malathion (Tuomainen et al., 2002). The higher proportion of exposure found on the legs in the studies by Cao et al., (2015) and Tuomainen et al. (2002), compared to the present study, could be due to the relatively taller crops sprayed in those two studies. The crop heights had means of 75 cm and 110 cm, respectively, compared to mean crop height of 42 cm in the present study (Table 1). Also, the pesticide in the present study was sprayed under irrigation conditions compared to the non-irrigation conditions with the studies by Cao et al. (2015) and Tuomainen et al. (2002). Consequently, part of the legs of applicators in the present study might have been protected from pesticide exposure by the irrigation water.

**Patterns on Upper and Lower Anatomical Regions of the Applicators**

The proportions of chlorpyrifos exposure on the upper (head, upper arms, lower arms, front abdomen and back abdomen) and lower (hands, upper legs, lower legs, and feet) anatomical regions of the applicators are presented in Figure 6.5. The figure shows that the upper anatomical region was the least contaminated (18% of TDE). The lower anatomical region accounted for 82% of TDE. With a maximum crop height of 80 cm (Table 6.1), it would be expected that less of the spray cloud would penetrate to the upper anatomical region. In addition, the applicators walked through densely planted crops that had been recently sprayed and the lower anatomical region would have had significant contact with pesticide soaked leaves.
The findings of the present study is consistent with similar studies (Castro Cano et al., 2000; Castro Cano et al., 2001; Tuomainen et al., 2002; Cao et al., 2015). The study reported by Cao et al. (2015) revealed that the level of exposure on the lower anatomical region (upper and lower legs) was about 76 to 79% of total exposure, compared to 9 to 10% for the upper anatomical region (head, chest, back, and arm). Similarly, the lower anatomical region received 64 to 79% of total exposure among applicutors who sprayed green peas (Castro Cano et al., 2000; Castro Cano et al., 2001). Tuomainen et al. (2002) also found among applicators who sprayed rose plants that exposure on the lower anatomical region constituted about 78% of total exposure. Conversely, exposure on the upper anatomical region could be higher than the lower anatomical regions, when spraying crops that are taller, as well as having more dense foliage in the upper portion. For instance, Hughes et al. (2008) found among applicators who sprayed maize crops, that exposure to deltamethrin on the upper anatomical region (head, torso, arms, and hands) was about 170 mL/h, compared to 140 mL/h on the lower anatomical region (upper and lower legs).
6.1.5 Factors Associated with Total Dermal Exposure

The results of the independent t-test analysis are reported in Table 3. Applicators who handled more insecticides (at least 150 mL) had significantly higher TDE (28±9.4 mg) compared to those that handled less than 150 mL of the insecticide (18±8.0 mg) ($p < 0.05$). Similar to this finding, a previous study (Hines et al., 2011) showed that the quantity of captan applied was a significant determinant of exposure. Comparable results have been reported by Phung et al. (2012a) and Aponso (2002). Applicators of the present study who sprayed taller crops (at least 35 cm) received significantly higher levels of exposure (29±12.5 mg) compared to those that sprayed crops less than 35 cm (20±6.2 mg) ($p < 0.05$). Tall rice crops were usually dense, allowing more contact with applicator’s clothing and body. Also, such crops required more pesticide to be sprayed, to effectively control pests, compared to shorter crops. Gao et al. (2014) has similarly
reported in a study which assessed chlorpyrifos exposure among applicators who sprayed maize crops, that spraying taller crops was significantly associated with higher levels of exposure.

Contrary to expectation, there was no significant difference in the exposure levels between applicators with at least Junior High School level of education and those that were not educated up to Junior High School ($p > 0.05$). In addition, applicators who had been trained on pesticide safety had similar levels of exposure to applicators that had not received any training on pesticide safety ($p > 0.05$). These findings suggest that being educated or trained on pesticide safety may not necessarily translate into reduced pesticide exposure. Fan et al. (2015) found that, because of fear of economic loss, vegetable and fruit farmers who were more knowledgeable and aware of pesticide safety used higher levels of pesticides, compared to their counterparts. It was similarly reported that, exposure prevention behaviours were poor among a group of tobacco farmers, although awareness of pesticides hazards was high (Damalas et al., 2006).

The type of shirt (long or short sleeve) worn by the applicators did not also influence the exposure levels significantly ($p > 0.05$), in contrast to the findings of previous studies (Blanco et al., 2005; Phung et al., 2012a) that showed that wearing long sleeve shirt was more protective against exposure. The clothing worn by most of the applicators in the present study were in relatively poor conditions, as have previously been reported elsewhere (Okello and Okello, 2010; Christie et al., 2015). Consequently, such clothing may not provide adequate protection against pesticide exposure.
Other factors that were not significantly associated with exposure were age of applicator, years of application, spraying duration, farm size, and whether or not there was spillage and leakages ($p > 0.05$).

Table 6.3: Factors Associated with Total Dermal Exposure (TDE) of Chlorpyrifos among Applicators on Rice Farms in Ghana ($n = 24$).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean TDE(mg)</th>
<th>SD</th>
<th>S.E.M</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age(years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 25</td>
<td>26</td>
<td>10.2</td>
<td>2.2</td>
<td>0.35</td>
<td>0.73</td>
</tr>
<tr>
<td>At least 25</td>
<td>24</td>
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<td>5.5</td>
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<td>-1.30</td>
<td>0.21</td>
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<td></td>
<td></td>
</tr>
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<td>Short sleeve</td>
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<tr>
<td><strong>Duration of spraying(minutes)</strong></td>
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<td></td>
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</tr>
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</tr>
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<td>24</td>
<td>11.1</td>
<td>3.0</td>
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<td></td>
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<td><strong>Incidence of spillage</strong></td>
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<td></td>
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<td></td>
</tr>
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<td>26</td>
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<td>1.9</td>
<td>0.24</td>
<td>0.81</td>
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<td>25</td>
<td>15.3</td>
<td>6.2</td>
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<td></td>
</tr>
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<td><strong>Farm size (ha)</strong></td>
<td></td>
<td></td>
<td></td>
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<td>0.70</td>
<td>0.50</td>
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<td>28</td>
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<td></td>
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<td><strong>Insecticide Quantity (mL)</strong></td>
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<td></td>
<td></td>
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<td>Less than 150</td>
<td>18</td>
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<td>3.6</td>
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<td>2.2</td>
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<td></td>
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<td><strong>Crop height (cm)</strong></td>
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<td>Less than 35</td>
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<td>2.40</td>
<td>0.03</td>
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<td>12.5</td>
<td>4.1</td>
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</tr>
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6.1.6 Absorbed Daily Dose (ADDD) of Chlorpyrifos from Dermal Exposure

The Total Dermal Exposure (TDE), dermal Absorbed Daily Dose (ADDD) and dermal Lifetime Average Daily Dose (LADD) of chlorpyrifos found with the applicators are presented in Table 6.4. ADDD is a measure of the daily chlorpyrifos exposure during a day’s spray event (acute exposure).

Using the TDE, ADDD of chlorpyrifos was estimated with the following equation reported in Section 4.5.8 and reproduced here as Equation 6.3:

\[
ADD_D = \frac{TDE \times DAF}{BW}
\]  

Equation 6.3

where, ADDD is the dermal Absorbed Daily Dose (μg/kg/day); TDE, Total Dermal Exposure (μg/day); DAF, Dermal Absorption Factor (%); and BW, Body Weight of each applicator (kg). DAF was estimated to be 4.3% (Meuling et al., 2005).

More discussion on DAF is provided in Section 4.5.7. Briefly, studies carried by (Nolan et al., 1984), (Griffin et al., 1999), and (Meuling et al., 2005) under slightly different experimental conditions to determine the DAF for chlorpyrifos yielded different values of 1.3%, 1.0% and 4.3%, respectively. In addition, a DAF of 9.6% (Thongsinthasak, 1991) and 3.0% (Geer et al., 2004) have been proposed, based on analysis of secondary data. With the present study, the DAF proposed by Meuling et al. (2005) was considered more appropriate considering the applied dose (50 μg/cm²) and duration (4
hours) of the experiment, which were closer to the spraying characteristics of the present study (Section 6.1.2 and 6.1.4). A full justification of this decision is given in Section 4.5.7.
Table 6.4 Total Dermal Exposure (TDE), Absorbed Daily Dose (ADD<sub>D</sub>) and Lifetime Average Daily Dose (LADD<sub>D</sub>) of Chlorpyrifos from Dermal Exposure with the Applicators (n = 24).

<table>
<thead>
<tr>
<th>Applicator</th>
<th>Total Dermal Exposure (µg/day)*</th>
<th>ADD&lt;sub&gt;D&lt;/sub&gt; (µg/kg/day)**</th>
<th>LADD&lt;sub&gt;D&lt;/sub&gt; (µg/kg/day)***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applicator 1</td>
<td>27,700</td>
<td>17.5</td>
<td>0.29</td>
</tr>
<tr>
<td>Applicator 2</td>
<td>24,200</td>
<td>17.3</td>
<td>0.29</td>
</tr>
<tr>
<td>Applicator 3</td>
<td>37,200</td>
<td>19.5</td>
<td>0.32</td>
</tr>
<tr>
<td>Applicator 4</td>
<td>11,800</td>
<td>7.5</td>
<td>0.12</td>
</tr>
<tr>
<td>Applicator 5</td>
<td>9,700</td>
<td>4.8</td>
<td>0.08</td>
</tr>
<tr>
<td>Applicator 6</td>
<td>22,100</td>
<td>15.3</td>
<td>0.25</td>
</tr>
<tr>
<td>Applicator 7</td>
<td>17,800</td>
<td>10.3</td>
<td>0.17</td>
</tr>
<tr>
<td>Applicator 8</td>
<td>29,500</td>
<td>18.7</td>
<td>0.31</td>
</tr>
<tr>
<td>Applicator 9</td>
<td>11,900</td>
<td>8.5</td>
<td>0.14</td>
</tr>
<tr>
<td>Applicator 10</td>
<td>48,900</td>
<td>22.1</td>
<td>0.36</td>
</tr>
<tr>
<td>Applicator 11</td>
<td>23,800</td>
<td>12.6</td>
<td>0.21</td>
</tr>
<tr>
<td>Applicator 12</td>
<td>37,700</td>
<td>28.0</td>
<td>0.46</td>
</tr>
<tr>
<td>Applicator 13</td>
<td>29,000</td>
<td>18.9</td>
<td>0.31</td>
</tr>
<tr>
<td>Applicator 14</td>
<td>27,500</td>
<td>17.1</td>
<td>0.28</td>
</tr>
<tr>
<td>Applicator 15</td>
<td>30,100</td>
<td>15.6</td>
<td>0.26</td>
</tr>
<tr>
<td>Applicator 16</td>
<td>31,000</td>
<td>18.5</td>
<td>0.30</td>
</tr>
<tr>
<td>Applicator 17</td>
<td>21,000</td>
<td>13.9</td>
<td>0.23</td>
</tr>
<tr>
<td>Applicator 18</td>
<td>12,800</td>
<td>10.2</td>
<td>0.17</td>
</tr>
<tr>
<td>Applicator 19</td>
<td>39,100</td>
<td>28.5</td>
<td>0.47</td>
</tr>
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<td>Applicator 20</td>
<td>36,300</td>
<td>26.0</td>
<td>0.43</td>
</tr>
<tr>
<td>Applicator 21</td>
<td>21,400</td>
<td>16.4</td>
<td>0.27</td>
</tr>
<tr>
<td>Applicator 22</td>
<td>31,500</td>
<td>15.9</td>
<td>0.26</td>
</tr>
<tr>
<td>Applicator 23</td>
<td>18,500</td>
<td>12.6</td>
<td>0.21</td>
</tr>
<tr>
<td>Applicator 24</td>
<td>18,100</td>
<td>14.7</td>
<td>0.24</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td><strong>25,800</strong></td>
<td><strong>16.3</strong></td>
<td><strong>0.27</strong></td>
</tr>
<tr>
<td><strong>S.D</strong></td>
<td><strong>9,900</strong></td>
<td><strong>6.0</strong></td>
<td><strong>0.1</strong></td>
</tr>
<tr>
<td><strong>S.E.M</strong></td>
<td><strong>2,020</strong></td>
<td><strong>1.2</strong></td>
<td><strong>0.02</strong></td>
</tr>
</tbody>
</table>

*TDE is the sum of chlorpyrifos measured from all anatomical regions.

**Estimated from Equation 5.1

***Estimated from Equation 5.2
The ADD with the applicators ranged from 4.8 to 28.5µg/kg/day, with a mean of 16.3µg/kg/day (±6.0). The mean acute exposure dose of the present study is about 7 times less than that of a similar dermal exposure assessment study conducted with applicators on rice farms in Thailand. In that study, a mean acute dose of 105.8µg/kg/day found with males was reported. Slightly high levels (mean of 119.0µg/kg/day) were found with female applicators (Lappharat et al., 2014). The authors explained that the higher body weight of the males (60.9kg) compared to that of the female (54.1kg) accounted for the relatively lesser dose of chlorpyrifos with the males. Usually, for a given pesticide concentration, estimated dose is inversely related to body weight.

In addition, the average size of rice farms in Thailand is about 2.5 hectares (ha) (Pornpratansombat et al., 2011), while that in the present study was about 0.5 ha (Table 6.1). The Thai applicators are therefore more likely to use more pesticides than the Ghanaian applicators, hence, the higher dose of chlorpyrifos reported in the Thai study.

The difference in the exposure dose between the Thai and Ghanaian applicators may also result partly from the different dermal exposure measurement approaches used in the two studies. Whereas the whole-body dosimetry approach was used in the present study, the patch method was used in the Thai study. With the patch method, patch samplers (made of absorbent materials) measuring about 10cm × 10cm are placed at various anatomical regions of the applicators. The patches are removed at the end of spraying activities and analysed for quantities of pesticide on them. The amount of pesticide found on each patch is then used to extrapolate to the amount of exposure for
the whole anatomical region where the patch was placed. Therefore, a major limitation of the patch method is the tendency to over- or underestimate pesticide exposure levels since pesticide depositions on one anatomical region may not be uniform (Schneider et al., 2000; Frenich et al., 2002; Behroozy, 2013).

6.1.7 Lifetime Average Daily Dose (LADD\textsubscript{D}) of Chlorpyrifos from Dermal Exposure

The LADD\textsubscript{D} of chlorpyrifos with the applicators was estimated with the following equation from Section 4.5.8, reproduced here as Equation 6.4:

\[
\text{LADD}_D = \frac{(\text{ADD}_D \times \text{EF} \times \text{ED})}{\text{AT}} \tag{Equation 6.4}
\]

where, \text{ADD}_D (\mu g/kg/day) is the dermal Absorbed Daily Dose of chlorpyrifos of the applicator; EF, the Exposure Frequency (Number of days per year); ED, the Exposure Duration (Work lifetime years); and AT, the Averaging Time [(life expectancy in years – application start age in years) x 365 days/ year].

LADD\textsubscript{D} measured the daily chlorpyrifos exposure during spray events over the working life of the applicators (chronic exposure). Chronic exposure to pesticides have been associated with adverse health effects on neurological and behavioural functions such as psychomotor, verbal memory, and coordination skills (Jamal et al., 2002; Munoz-Quezada et al., 2016). More debilitating chronic effects include Parkinson’s disease Alzheimer’s disease and cancers (Bassil et al., 2007; Dhillon et al., 2008; Yan et al.,
2016). Despite the importance of chronic exposure, majority of the studies that evaluated pesticides exposure among agricultural applicators focused on acute exposure (Ngo et al., 2010). This is probably because evaluation of chronic exposure may require repeated measurements for a long period.

However, chronic exposure to pesticides can be extrapolated based on acute exposure measurements (Ngo et al., 2010; Phung et al., 2012a). Assuming that the current pattern of pesticides use with the applicators in this study will be similar to future use patterns, chronic exposure dose for each applicator was estimated based on a single acute exposure dose, averaged over the expected life time (Equation 6.4). The estimated chronic exposure dose (LADD_D) found with the applicators ranged from 0.08 to 0.47µg/kg/day, with a mean (±S.D) of 0.3µg/kg/day (±0.1) (Table 6.4). No comparable study evaluating chronic exposure to chlorpyrifos based on dermal assessment was identified in the scientific literature.

### 6.1.8 Summary

The present study used the whole-body dosimetry technique to evaluate dermal exposure to chlorpyrifos among applicators on rice farms in a typical farming community in Ghana. Chlorpyrifos TDE among the median exposed and the 5% highly exposed groups were 24 mg and 48 mg, respectively. These translated into percentage UE values of 0.03% and 0.06% among the median exposed and the 5% highly exposed groups, respectively. These were much higher than the UE value of a comparable pesticide handler scenario of USEPA’s unit exposure surrogate reference database. In
many developing countries, such as Ghana, pesticide exposure and risk assessment studies are usually not carried out as part of the processes for registering new pesticides for several reasons including financial and logistical challenges. Such countries may therefore rely on exposure models and databases from developed countries to evaluate pesticides. However, the findings of the present study clearly demonstrate that such an approach for pesticide exposure and risk assessment could be problematic because of differences in pesticide UE values between developed and developing countries.

The mean ADD\(_D\) (acute exposure) of chlorpyrifos, estimated from TDE of the applicators was determined to be 16\(\mu\)g/kg/day, with a standard deviation of ±6.0 \(\mu\)g/kg/day; while the mean LADD\(_D\) (chronic exposure) of chlorpyrifos was 0.3\(\mu\)g/kg/day, with a standard deviation of ±0.1\(\mu\)g/kg/day.

Overall, the hands were the most contaminated anatomical region of the applicators both in terms of proportion of exposure (39% of TDE) and skin loading (13 \(\mu\)g/cm\(^2\)). Also, the lower anatomical region was more contaminated (82% of TDE) compared to the upper anatomical region (18% of TDE). However, these results should be interpreted with caution, owing to the small sample (n=4) used to determine the pattern of exposure.

The levels of chlorpyrifos exposure with the applicators were significantly influenced by the quantity of insecticide applied and the height of the crops sprayed (p < 0.05). These findings suggest that actions that may be taken to significantly reduce pesticide exposure among applicators may include protecting the hands and the lower anatomical
regions with appropriate PPE; and reducing the quantities of pesticides handled by applicators. Also, other practices such as washing the hands, changing farm clothing, and bathing immediately after spraying may help to reduce exposure.

With the use of the whole-body dosimetry technique, the present study has provided important information on the magnitude, pattern, and determinants of dermal exposure to chlorpyrifos in a tropical country. The pesticide UE data of the present study can be used to estimate dermal pesticide exposure under similar pesticide use scenarios.
6.2 Overall Chlorpyrifos Exposure Estimated from Urinary TCP with the Applicators

6.2.1 Introduction

The conceptual framework of this research, based on the four-step health risk assessment framework of the United States’ National Research Council (USEPA, 2000; NRC, 2009), is shown in Figure 4.1 of Section 4.2 and repeated in this section as Figure 6.6. The figure illustrates how the chapters and sections of the research fit into the conceptual framework. The main objectives of the overall research were to:

1. Identify hazardous pesticides and practices associated with the use of pesticides among applicators;
2. Assess the levels of chlorpyrifos exposure among applicators;
3. Evaluate the patterns of dermal exposure to chlorpyrifos among applicators;
4. Review the dose-response relationship of chlorpyrifos exposure and adverse effects;
5. Characterize the risks of adverse health effects due to chlorpyrifos exposure among applicators;

The outcome of the hazard identification study among the farmers is reported in Chapter 5. The study showed that all the farmers applied pesticides to control pests and 83% reported using chlorpyrifos. The initial assessment of chlorpyrifos exposure based on dermal dosimetry showed that the applicators were exposed to high levels of chlorpyrifos with mean chlorpyrifos Absorbed Daily Dose (ADD) of 16.3 µg/kg/day from dermal exposure. Although the dermal dosimetry may give good estimates of
exposure, it does not measure the actual absorbed dose. Also, the approach does not account for exposure from other routes.

To address these considerations, an exposure evaluation based on urinary 3, 5, 6-trichloro-2-pyridinol (TCP) was carried out with the applicators (Section 4.6). TCP is the primary metabolite of chlorpyrifos (Nolan et al., 1984). In humans, it is found mainly in the urine of exposed individuals. Urinary TCP has therefore been widely used as a biomarker to evaluate exposure to chlorpyrifos (Baker et al., 2005; Alexander et al., 2006; Farahat et al., 2011; Phung et al., 2012b). A major advantage of the use of TCP is that, it incorporates exposure from all routes and therefore gives an overall measure of exposure (Albertini et al., 2006; Barr and Angerer, 2006).

The objective of Section 6.2, highlighted with blue colour in Figure 6.6, is to present the results and discussion of the study conducted to evaluate exposure to chlorpyrifos among the applicators, based on urinary TCP assessment. Section 6.2 addresses objective 2 of the whole research. The information obtained from this exposure evaluation will be used in Section 8.2 of the research to characterize risk of adverse health effect.
Figure 6.6: The Section on Overall Chlorpyrifos Exposure Estimated from Urinary TCP (highlighted with blue colour in the overall research framework) (see Figure 4.1 in Section 4.2).
6.2.2 Personal Characteristics of the Applicators and Observed Field Factors during Application

The personal characteristics of the applicators and field factors were recorded during the spray event. All the applicators were male aged between 23 to 53 years (mean, 40 years). Fifty eight percent of the applicators were educated up to Junior High School (JHS) level, whereas the rest (42%) had education above this level. The applicators had used insecticides for between 5 and 32 years with a mean of 16 years.

The field factors observed during the spraying event are presented in Table 6.5. Most the applicators wore long trousers (95%) and short sleeve shirts (52%). Two of the applicators (9%) used safety glasses during the spraying while the rest (91%) did not use any PPE. Incidences of pesticide leakage and spillage were observed among 52% and 81% of the applicators, respectively. The size of the farms treated ranged from 0.2 to 1.0 ha (mean, 0.6 ha), whereas the crop height varied between 13 to 100 cm (mean 49 cm). The quantities of chlorpyrifos Emulsifiable Concentrate (EC) applied ranged from 88 to 600 mL (mean 224 mL), while the duration of spraying was between 25 to 224 min (mean 82 min.).
<table>
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<th>Type of Shirt</th>
<th>Type of PPE</th>
<th>Leaky Tank</th>
<th>Spillage</th>
<th>Farm Size (ha)</th>
<th>Crop Height (cm)</th>
<th>Insecticide Quantity (mL)</th>
<th>Spraying Duration (min)</th>
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<td>100</td>
<td>175</td>
<td>100</td>
</tr>
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<td>Yes</td>
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<td>40</td>
<td>200</td>
<td>90</td>
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<td>Yes</td>
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<td>50</td>
<td>100</td>
<td>60</td>
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<td>18</td>
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<td>158</td>
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<td>12</td>
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<td>Long sleeve</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>0.2</td>
<td>35</td>
<td>88</td>
<td>25</td>
</tr>
<tr>
<td>13</td>
<td>Long</td>
<td>Short sleeve</td>
<td>Safety glasses</td>
<td>Yes</td>
<td>Yes</td>
<td>0.5</td>
<td>20</td>
<td>150</td>
<td>38</td>
</tr>
<tr>
<td>14</td>
<td>Long</td>
<td>Short sleeve</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>0.8</td>
<td>30</td>
<td>400</td>
<td>100</td>
</tr>
<tr>
<td>15</td>
<td>Long</td>
<td>Long sleeve</td>
<td>None</td>
<td>No</td>
<td>Yes</td>
<td>0.4</td>
<td>30</td>
<td>150</td>
<td>46</td>
</tr>
<tr>
<td>16</td>
<td>Long</td>
<td>Short sleeve</td>
<td>None</td>
<td>Yes</td>
<td>No</td>
<td>0.6</td>
<td>100</td>
<td>175</td>
<td>100</td>
</tr>
<tr>
<td>17</td>
<td>Long</td>
<td>Long sleeve</td>
<td>None</td>
<td>Yes</td>
<td>Yes</td>
<td>0.5</td>
<td>30</td>
<td>150</td>
<td>40</td>
</tr>
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<td>18</td>
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<td>Long sleeve</td>
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<td>Yes</td>
<td>Yes</td>
<td>0.4</td>
<td>35</td>
<td>150</td>
<td>51</td>
</tr>
<tr>
<td>19</td>
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<td>Long sleeve</td>
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<td>Yes</td>
<td>0.8</td>
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<td>150</td>
<td>50</td>
</tr>
<tr>
<td>20</td>
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<td>Long sleeve</td>
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<td>No</td>
<td>No</td>
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<td>80</td>
<td>200</td>
<td>130</td>
</tr>
<tr>
<td>21</td>
<td>Long</td>
<td>Long sleeve</td>
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<td>Yes</td>
<td>Yes</td>
<td>1.0</td>
<td>70</td>
<td>600</td>
<td>224</td>
</tr>
</tbody>
</table>

Summary

Long (95%) Short (5%)
Long sleeve (52%) Short sleeve (48%)
PPE (9%) No PPE (91%)
Yes (52%) No (48%)
Yes (81%) No (19%)

Mean (0.61) S.D (0.26) S.E.M (0.06)
Mean (49) S.D (29) S.E.M (6)
Mean (224) S.D (139) S.E.M (30)
Mean (82) S.D (48) S.E.M (10)
6.2.3 Urinary Creatinine Levels of the Applicators

Urinary creatinine levels were determined and used to normalize the urinary TCP levels of the applicators (details provided in Section 4.7.6). The daily urinary creatinine levels found for the five-day sampling period are presented in Table 6.6. The mean creatinine levels for each applicator ranged from 0.3 g/L to 2.1 g/L. These levels were similar to those among applicators from Costa-Rica (0.1–4 g/L) (Park et al., 2008) and Vietnam (0.5 – 3.0 g/L) (Phung, 2012).

Only one urine sample had creatinine level (0.2 g/L) below the WHO’s recommended creatinine range (0.3 g/L - 3 g/L) for biological monitoring of chemical pollutants (WHO, 1996). Creatinine concentration less than 0.3 g/L is regarded too dilute, whereas concentration more than 3 g/L is regarded too concentrated. However, Barr et al. (2005) have suggested a review or abolition of the lower limit of the WHO’s creatinine recommendation because improvement in the limits of detection of analytical methods recently, allows toxicants in dilute urine samples to be adequately quantified. Therefore, the urine sample in the present study that had creatinine level less than the lower limit of the WHO’s recommendation was not excluded from the data analysis.
Table 6.6 Urinary Creatinine (g/L) Levels of Applicators on Rice Farms in Ghana (n=21)

<table>
<thead>
<tr>
<th>Applicator</th>
<th>Background Creatinine</th>
<th>Post-application Creatinine</th>
<th>Mean (±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Day 0</td>
<td>Day 1</td>
</tr>
<tr>
<td>01</td>
<td>0.7</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td>02</td>
<td>0.7</td>
<td>1.2</td>
<td>1.3</td>
</tr>
<tr>
<td>03</td>
<td>1.5</td>
<td>0.6</td>
<td>1.4</td>
</tr>
<tr>
<td>04</td>
<td>1.1</td>
<td>1.2</td>
<td>2.0</td>
</tr>
<tr>
<td>05</td>
<td>1.0</td>
<td>0.9</td>
<td>1.1</td>
</tr>
<tr>
<td>06</td>
<td>1.1</td>
<td>0.8</td>
<td>1.2</td>
</tr>
<tr>
<td>07</td>
<td>0.3</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>08</td>
<td>0.6</td>
<td>0.5</td>
<td>0.7</td>
</tr>
<tr>
<td>09</td>
<td>1.5</td>
<td>2.5</td>
<td>2.4</td>
</tr>
<tr>
<td>10</td>
<td>1.2</td>
<td>1.6</td>
<td>1.1</td>
</tr>
<tr>
<td>11</td>
<td>1.1</td>
<td>1.4</td>
<td>1.1</td>
</tr>
<tr>
<td>12</td>
<td>1.7</td>
<td>3.0</td>
<td>2.0</td>
</tr>
<tr>
<td>13</td>
<td>0.9</td>
<td>1.2</td>
<td>1.1</td>
</tr>
<tr>
<td>14</td>
<td>0.7</td>
<td>1.0</td>
<td>0.9</td>
</tr>
<tr>
<td>15</td>
<td>0.9</td>
<td>0.8</td>
<td>1.0</td>
</tr>
<tr>
<td>16</td>
<td>0.8</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>17</td>
<td>2.0</td>
<td>1.2</td>
<td>1.1</td>
</tr>
<tr>
<td>18</td>
<td>0.7</td>
<td>0.9</td>
<td>1.0</td>
</tr>
<tr>
<td>19</td>
<td>1.6</td>
<td>1.1</td>
<td>1.5</td>
</tr>
<tr>
<td>20</td>
<td>2.0</td>
<td>0.4</td>
<td>0.6</td>
</tr>
<tr>
<td>21</td>
<td>1.1</td>
<td>1.6</td>
<td>1.4</td>
</tr>
</tbody>
</table>

NA – Data not available.
6.2.4 Urinary TCP Levels of the Applicators

The creatinine-normalized background (baseline) and post-application urinary TCP levels found with the applicators in the study are presented in Table 6.7. Out of a total of 126 urine samples obtained from the applicators, 14 (12 background samples and 2 post-application samples) had TCP levels below the Limit of Quantification (LOQ) (5µg/L). Generally, measurements below this limit does not necessarily imply that there is zero exposure (Solomon et al., 2005). Thus, these samples were assigned a value of half the LOQ (Beal, 2001).

Two applicators (numbers 2 and 9 in Table 6.7) were observed to apply significant quantities (200 and 250 mL) of chlorpyrifos (Dursban, 480g/L EC) with similar spraying practices to the other applicators. However, they appeared not be exposed based on their post-application TCP levels, which were less than their respective background levels. The chlorpyrifos formulation used by these applicators was therefore suspected to be adulterated or another product substituted. This is common in farming communities in Ghana (MOFA, 2011b). Also, applicator number 18 had background TCP level of 124 µg TCP/g creatinine, which was about 36 times higher than the mean background TCP of the rest of the applicators. It is suggested that the high background TCP found with applicator number 18 might be due to non-reported use of chlorpyrifos product the week prior to the urine sampling, contrary to the requirements of the study. As a result of these considerations, the post-application TCP from the three applicators (marked with asterisk symbol in Table 2) were excluded from the statistical analysis of the study. The exclusion criteria applied in this study were similarly used in previous studies (Ross et al., 2008; Scher et al., 2008).
The background urinary TCP levels ranged from 1 to 36 µg TCP/g creatinine with a median of 3 µg TCP/g creatinine and a mean of 6 (±8) µg TCP/g creatinine. With post-application urinary TCP, the levels found ranged from 11 to 1,550 µg TCP/g creatinine, with a median of 105 µg TCP/g creatinine and a mean of 350 (±480) µg TCP/g creatinine.
Table 6.7: Urinary TCP (µg/g creatinine) Levels of Applicators on Rice Farms in Ghana (n = 21)

<table>
<thead>
<tr>
<th>Applicator</th>
<th>Background TCP</th>
<th>Post-application Urinary TCP (corrected for background TCP)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0</td>
<td>Day 1</td>
</tr>
<tr>
<td>01</td>
<td>4</td>
<td>41</td>
</tr>
<tr>
<td>02*</td>
<td>7</td>
<td>-2</td>
</tr>
<tr>
<td>03</td>
<td>2</td>
<td>38</td>
</tr>
<tr>
<td>04</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>05</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>06</td>
<td>2</td>
<td>9</td>
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<tr>
<td>07</td>
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<tr>
<td>08</td>
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<td>9</td>
</tr>
<tr>
<td>09*</td>
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<td>423</td>
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<td>34</td>
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</tr>
<tr>
<td>15</td>
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<td>24</td>
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<td>16</td>
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<td>136</td>
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<tr>
<td>20</td>
<td>4</td>
<td>139</td>
</tr>
<tr>
<td>21</td>
<td>36</td>
<td>372</td>
</tr>
</tbody>
</table>

Minimum     | 1     | 3     | 2     | 1     | 1     | 2     | 11    |
Median       | 3     | 29    | 34    | 28    | 20    | 5     | 105   |
Mean         | 6     | 83    | 108   | 72    | 54    | 40    | 350   |
SD           | 8     | 126   | 145   | 96    | 74    | 53    | 480   |
SEM          | 2     | 30    | 34    | 23    | 18    | 13    | 110   |
Maximum      | 36    | 420   | 470   | 301   | 230   | 142   | 1550  |

*The results from these applicators were excluded from further analysis for reasons outlined in Section 6.2.5.
6.2.5 Elimination Half-life of Chlorpyrifos Found with the Applicators

The time-concentration profile of Absorbed Daily Dose of chlorpyrifos (ADD$_A$) estimated (Section 4.7.7) from the TCP levels of the applicators, following a spray event, is shown in Figures 6.7 and 6.8. The mean ADD$_A$ of chlorpyrifos peaked at 5.5 µg/kg/day on day one after which the level rapidly declined on the subsequent days. Similar excretion patterns have been reported in previous studies (Mandel et al., 2005; Meuling et al., 2005; Phung et al., 2012b). The decline of chlorpyrifos with time was found to follow first-order kinetics with the following equation from Figure 6.8:

$$\ln\text{ADD} = -0.327\text{Time} + 2 \quad (R^2 = 0.99, \ p < 0.01) \quad \text{Equation 6.5}$$

The first-order elimination half-life ($t_{1/2}$) of chlorpyrifos with the applicators was determined by using the elimination rate constant ($k$, 0.327) from Equation 6.5, and then applying the equation, $t_{1/2} = 0.693/k$ (Toutain and Bousquet-Melou, 2004). Thus, $t_{1/2} = 2.1$ days (50 hours).

The half-life of chlorpyrifos determined in the present study is higher than those reported in previous studies, which ranges from 27 to 43 hours (Nolan et al., 1984; Griffin et al., 1999; Williams et al., 2004; Meuling et al., 2005; Wang et al., 2016). The longer half-life value found in the present study could be attributable to several factors. For instance, after spraying, the applicators were observed bathing without soap and partially changed their clothes. These practices might leave significant amounts of chlorpyrifos residues on the skin for many hours after spraying. With an octanol/water
partition coefficient (log $K_{OW}$) of 5.0 at 25°C (WHO, 2009), chlorpyrifos would generally exhibit lipophilic properties and therefore has the potential to accumulate in the lipid-rich stratum corneum of applicators (Griffin et al., 2000; Meuling et al., 2005; Moore et al., 2014). Also, unlike technical grade chlorpyrifos used in the studies by Nolan et al. (1984), Griffin et al. (1999), and Meuling et al. (2005), formulated chlorpyrifos usually contains inert ingredients which may enhance the adsorptive capacity on cotton clothing of applicators and thereby make decontamination difficult (Laughlin et al., 1985; Cox and Surgan, 2006).

Figure 6.7: Time-Absorbed Dose (Mean $ADD_A \pm S.E.M$) Profile of Chlorpyrifos (Corrected for Background) Found with Applicators on Rice Farms in Ghana After One Application ($n=n18$)
With a half-life of 50 hours in the body, the level of post-application chlorpyrifos with the applicators would be expected to return to background levels in about 10 days after exposure (i.e. 5 half-lives). These findings have important implications for the design of biomonitoring programs to evaluate chlorpyrifos levels among applicators. Exposure to chlorpyrifos has often been evaluated based on urinary TCP levels obtained from the start of application up to 120 hours (5 days) post-application or less (34 hours) (Nolan et al., 1984; Griffin et al., 1999; Williams et al., 2004; Mandel et al., 2005; Meuling et al., 2005; Alexander et al., 2006; Rodriguez et al., 2006; Phung et al., 2012b). The
measurements obtained within these sampling periods would likely under-estimate the levels of chlorpyrifos exposure, since its elimination would still be ongoing beyond these time periods. The findings of the present study also imply that, to accurately measure background exposure levels of chlorpyrifos, applicators should not apply the insecticide for at least 10 days prior to urine samples being taken.

6.2.6 Lifetime Average Daily Dose of Chlorpyrifos from Background Exposure Found with Applicators

The Lifetime Average Daily Dose of chlorpyrifos from background exposure (LADD_B) for the applicators estimated from the background urinary TCP levels (Table 6.7) are presented in Table 6.10. Unlike LADD_D (Section 4.5.8) and LADD_A (Section 4.6.8), LADD_B was not estimated from ADD. Rather, LADD_B was a direct measurement of daily background exposure. Therefore, there was no need to apply estimation factors such as Exposure Frequency (EF), Exposure Duration (ED) and Averaging Time (AT), as with LADD_D and LADD_A. The LADD_B values were therefore estimated using the following equation from Section 4.7.7, reproduced in this Section as Equation 6.6:

\[
LADD_B (\mu g/kg/day) = \left[ C \times Cn \times CF \times \left( \frac{MW_{CPF}}{MW_{TCP}} \right) \right]/BW \quad \text{Equation 6.6}
\]

where, LADD_B is the Lifetime Average Daily Dose of chlorpyrifos from background exposure (\mu g/kg/day); C, the concentration of TCP excreted per day (\mu g/g); Cn, expected mass of creatinine excreted per day(g/day); CF, correction factor of 100/70 for urinary TCP (about 70% of chlorpyrifos is excreted as TCP in urine ) (Nolan et al., 1984); MW_{CPF}, the molecular weight of chlorpyrifos (350.6g/mol); MW_{TCP} the
molecular weight of TCP (198.5g/mol); and BW, the body weight of each applicator (kg).

The LADD$_B$ of this study ranged from 0.05 to 2 µg/kg/day, with a median of 0.2 µg/kg/day and mean (± S.D) of 0.3 (± 0.4) µg/kg/day. These levels are similar to those found among applicators in Sri-Lanka (0.01 to 1.22 µg/kg/day) and Vietnam (0.03 to 1.98 µg/kg/day) (Aponso, 2002; Phung et al., 2012a), possibly reflecting comparable dietary exposure levels and household chlorpyrifos use practices. A global evaluation of chlorpyrifos exposure has shown that background levels do not usually vary widely between countries (Marasinghe et al., 2014).

Background levels of pesticides are usually attributable to common non-occupational sources such as food, drinking water, and household application (Macintosh et al., 2001; Whyatt et al., 2002; Eaton et al., 2008). Therefore, background pesticides levels among members of a population can be similar. However, a study by Bakke et al. (2009) that evaluated exposure to 2,4-D amongst others, suggested that farmers could have background exposure through additional sources. In that study, farmers had significantly elevated background levels of 2,4-D during all seasons, compared to non-farmers (2 µg 2,4-D/g creatinine and 0.2 µg 2,4-D/g creatinine, respectively; p<0.05). Additional background exposure with farmers, may occur through storage of unused pesticides in household premises, household use of empty pesticide containers and washing of pesticide-contaminated farm clothing. Moreover, spray drift can lead to higher background levels of pesticides among farmers and people living on or near agricultural areas (Ward et al., 2006; Coronado et al., 2011).
6.2.7 Absorbed Daily Dose of Chlorpyrifos from Application Exposure (ADD$_A$) Found with Applicators

Absorbed Daily Dose of chlorpyrifos from application exposure (ADD$_A$) was similarly calculated from Equation 4.3, using the post-application urinary TCP levels (Table 6.7). The ADD$_A$ levels ranged from 0.7 to 74 µg/kg/day, with a median of 6 µg/kg/day and a mean ($\pm$ S.D) of 19 ($\pm$ 24) µg/kg/day (Table 6.10). The median ADD$_A$ (6 µg/kg/day) was 30-fold higher than the median LADD$_B$ (0.2 µg/kg/day), which indicates that occupational exposure significantly elevated chlorpyrifos levels among the applicators.

The median ADD$_A$ of this study is generally comparable to the levels found with applicators from other developing countries such as Sri-Lanka (5 µg/kg/day) (Aponso, 2002), Nicaragua (9 µg/kg/day) (Dowling et al., 2005), and Vietnam (8 µg/kg/day) (Phung et al., 2012b). Conversely, the mean ADD$_A$ (19 µg/kg/day) of the present study is 7-fold less than that (141 µg/kg/day) found with applicators in Egypt (Farahat et al., 2010). This is not unexpected because the levels found in the present study were for one spray event, compared to 16 consecutive days of spray events in the case of the Egyptian applicators.

However, the mean ADD$_A$ (19 µg/kg/day) of the present study was 10-fold higher than that (2 µg/kg/day) found with applicators from the USA (Alexander et al., 2006). These differences are probably due to differences in pesticide handling practices among applicators in the present study and the applicators in USA. For instance, whereas none of the applicators in the present study used hand gloves, close to 60% of the applicators from USA used hand gloves. Moreover, the spraying in USA usually involved the
applicators operating from an enclosed cab on a tractor. They would thus have had much lower risk of exposure compared to the applicators in the present study who used back packs with hand-held spraying wands.

Table 6.8: Absorbed Doses (µg/kg/day) of Chlorpyrifos with Applicators on Rice Farms in Ghana (n = 18).

<table>
<thead>
<tr>
<th>Applicator* ID</th>
<th>LADD_B</th>
<th>LADD_A</th>
<th>ADD_A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.17</td>
<td>0.42</td>
<td>16.0</td>
</tr>
<tr>
<td>3</td>
<td>0.08</td>
<td>0.09</td>
<td>5.8</td>
</tr>
<tr>
<td>4</td>
<td>0.25</td>
<td>0.01</td>
<td>0.9</td>
</tr>
<tr>
<td>5</td>
<td>0.14</td>
<td>0.01</td>
<td>0.7</td>
</tr>
<tr>
<td>6</td>
<td>0.13</td>
<td>0.06</td>
<td>2.8</td>
</tr>
<tr>
<td>7</td>
<td>0.43</td>
<td>0.21</td>
<td>13.4</td>
</tr>
<tr>
<td>8</td>
<td>0.19</td>
<td>0.03</td>
<td>2.0</td>
</tr>
<tr>
<td>10</td>
<td>0.11</td>
<td>0.15</td>
<td>14.6</td>
</tr>
<tr>
<td>11</td>
<td>0.40</td>
<td>0.72</td>
<td>70.9</td>
</tr>
<tr>
<td>12</td>
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<td>14.2</td>
</tr>
<tr>
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<td>0.15</td>
<td>0.08</td>
<td>5.1</td>
</tr>
<tr>
<td>14</td>
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<td>0.71</td>
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</tr>
<tr>
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<td>0.08</td>
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<td>0.11</td>
<td>5.3</td>
</tr>
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<td>0.03</td>
<td>1.9</td>
</tr>
<tr>
<td>19</td>
<td>0.21</td>
<td>0.04</td>
<td>2.3</td>
</tr>
<tr>
<td>20</td>
<td>0.24</td>
<td>0.84</td>
<td>53.7</td>
</tr>
<tr>
<td>21</td>
<td>1.94</td>
<td>1.17</td>
<td>74.4</td>
</tr>
</tbody>
</table>

**Minimum**  | 0.05  | 0.01  | 0.7   |
**Median**    | 0.2   | 0.1   | 6     |
**Mean**      | 0.3   | 0.3   | 19    |
**S. D**      | 0.4   | 0.3   | 24    |
**S.E.M**     | 0.1   | 0.07  | 6     |
**Maximum**   | 2     | 1     | 74    |

* Results of the applicators 2, 8, and 18 were excluded for reasons outlined in Section 6.2.5.
6.2.8 Life-time Absorbed Daily Dose of Chlorpyrifos from Application Exposure (LADD<sub>A</sub>)

LADD<sub>A</sub> of chlorpyrifos was estimated from ADD<sub>A</sub> to evaluate long term occupational exposure to chlorpyrifos among applicators in the study. The estimation was done using the following equation from Section 4.7.7, reproduced in this Section as Equation 6.2.3:

\[
\text{LADD}_A = \frac{(\text{ADD}_A \times \text{EF} \times \text{ED})}{\text{AT}} \quad \text{Equation 6.7}
\]

where, ADD<sub>A</sub> (µg/kg/day) is the Absorbed Daily Dose of chlorpyrifos from application exposure; EF, the Exposure Frequency (number of applications days per year); ED, the Exposure Duration (work lifetime years); and AT, the Averaging Time [(life expectancy in years – application start age in years) x 365 days/year].

The LADD<sub>A</sub> of chlorpyrifos this study ranged from 0.01 to 1 µg/kg/day, with a median of 0.1 µg/kg/day and a mean (± S.D) of 0.3 (±0.3) µg/kg/day (Table 6.10). The study by Phung et al. (2013) is the only investigation from the scientific literature that has evaluated chronic exposure to chlorpyrifos among agricultural applicators. The median LADD<sub>A</sub> in the present study is slightly lower than that (0.31 µg/kg/day) found with applicators on rice farms in Vietnam (Phung et al., 2013). This difference could be explained by differences in exposure frequencies between the two applicator groups. The applicators in the present study apply chlorpyrifos about 6 times in a year (3 applications per crop season × 2 crop seasons in a year), whereas the Vietnamese applicators apply chlorpyrifos 10 times in a year (Phung, 2012).
6.2.9 Factors Associated with Absorbed Daily Dose of Chlorpyrifos from Application Exposure (ADD$_{A}$)

The relationships between field factors and Absorbed Daily Dose from Application Exposure (ADD$_{A}$) were statistically evaluated. The results of the Spearman ρ correlation and Mann-Whitney U tests are presented in Tables 6.11 and 6.12, respectively. Table 6.11 shows that the quantities of insecticide formulation applied were statistically related to the ADD$_{A}$ levels. Increases in insecticide quantity significantly correlated with increases in ADD$_{A}$ ($r = 0.59$, $p < 0.05$).

Similarly, Phung et al. (2012a) found among rice farmers that, the quantities of chlorpyrifos applied significantly influenced the levels of ADD$_{A}$ ($r = 0.69$, $p < 0.05$). A stepwise multiple linear regression analysis in that study showed that, ADD$_{A}$ increased by 0.48 µg/kg/day per gram increase of chlorpyrifos applied. Likewise, Bakke et al. (2009) found among corn farmers that the quantity (kg) of pesticide applied was a predictor ($\beta = 0.008$, $p < 0.05$) of atrazine exposure, measured as urinary atrazine mercapturate (AZM). In a related study based on previous studies and expert judgement, Marquart et al. (2003) also reported that the quantity of pesticide applied influences the levels of dermal exposure.

Spraying duration was also positively associated with ADD$_{A}$ levels ($r = 0.59$, $p < 0.05$). (Phung et al., 2012a) similarly found that the number of hours spent spraying insecticides was positively associated with the level of exposure ($r = 0.69$). Also, Hines and Deddens (2001) demonstrated that spray duration was a significant determinant of urinary TCP levels and chlorpyrifos concentration in the ambient air among termiticide applicators ($\beta = 0.002$, $p < 0.001$ and $\beta = 0.006$, $p < 0.001$, respectively). A possible
explanation for the findings of the present study is that, extended spraying duration normally allows more time for pesticide residues deposited on the skin to be absorbed, particularly for pesticides such as chlorpyrifos that exhibit lipophilic properties (Griffin et al., 2000; Meuling et al., 2005). In evaluating dermal absorption and distribution of organophosphate insecticides with in-vitro human skin model, Moore et al. (2014) found that there was an increased skin reservoir because of extended exposure duration. This increased reservoir would be available for later systemic absorption. Another possible reason is that, farmers who spray for longer duration may experience more sweating, which may in turn enhance skin absorption of pesticides (Meuling et al., 1997; Williams et al., 2004).

The number of spray tanks applied by the applicators was also positively correlated with the levels of ADDA ($r = 0.53$, $p > 0.05$). Some research has shown that hand contamination can be the highest contributor to exposure among pesticide applicators (Machera, 2003; Baldi et al., 2006; Vitali et al., 2009), with the most hand contamination occurring during mixing and loading of pesticides into spray tanks (Gao et al., 2014; Kim et al., 2014). None of the applicators in the present study used hand gloves, a situation that predisposed them to direct hand contamination. Alexander et al. (2006) similarly found among licensed applicators who applied liquid chlorpyrifos with boom sprayers that, urinary TCP levels significantly increased with increase in the number of spray loads applied. The mean urinary TCP levels found among applicators who used 1 to 2, 3 to 5, and more than 5 spray loads were 24, 29 and 76 µg TCP/L urine, respectively ($p < 0.05$).
Farm size, crop height, type of shirt, incidence of leakage, and incidence of spillage, however, were all not statistically associated with ADDₐ levels ($p > 0.05$) (Tables 6.8 and 6.9). In contrast to these findings, area treated (Marquart et al., 2003; Blanco et al., 2005), crop height (Gao et al., 2014) and type of shirt (short or long sleeve) (Blanco et al., 2005; Phung et al., 2012a) have been found to be significantly associated with pesticide exposure.

Some of the independent variables were found to be significantly associated with one another. Insecticide quantity positively correlated with spraying duration, farm size and the number of spray tanks applied ($p > 0.01$). Spray duration was also positively related with farm size, crop height and the number of spray tanks applied ($p > 0.05$). Moreover, the number of spray tanks applied was positively associated with farm size ($p > 0.01$). Consequently, some of the identified associations between ADDₐ levels and the independent variables in this study can be secondary and may require multiple linear regression analysis to identify the primary associations. However, such analysis was not carried out, owing to the small sample size of the study. Generally, a minimum of 50 observations is required for multiple linear regression analysis (Van Voorhis and Morgan, 2007).
Table 6.9: Spearman $\rho$ Correlation Coefficient ($r$) Between $ADD_A$ Levels and Independent Continuous Variables ($n = 18$).

<table>
<thead>
<tr>
<th>Variable</th>
<th>$ADD_A$ ($\mu g/kg/day$)</th>
<th>Insecticide Formulation Quantity (mL)</th>
<th>Spraying Duration (min)</th>
<th>Farm Size (ha)</th>
<th>Crop Height (cm)</th>
<th>No. of Spray Tanks</th>
</tr>
</thead>
<tbody>
<tr>
<td>$ADD_A$ ($\mu g/kg/day$)</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insecticide Formulation Quantity (mL)</td>
<td>0.59*</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spraying Duration (min)</td>
<td>0.59*</td>
<td>0.87**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Farm Size (ha)</td>
<td>0.19</td>
<td>0.76**</td>
<td>0.65**</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crop Height (cm)</td>
<td>0.27</td>
<td>0.15</td>
<td>0.47*</td>
<td>0.26</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>No. of Spray Tanks</td>
<td>0.53*</td>
<td>0.99**</td>
<td>0.87**</td>
<td>0.76**</td>
<td>0.15</td>
<td>1</td>
</tr>
</tbody>
</table>

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

Table 6.10: Mann-Whitney U Test of Difference in $ADD_A$ ($\mu g/kg/day$) Levels Between Groups for Categorical Variables ($n = 18$).

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Mean Rank</th>
<th>Z</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Shirt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short sleeve</td>
<td>8</td>
<td>10.0</td>
<td>-0.36</td>
<td>0.72</td>
</tr>
<tr>
<td>Long sleeve</td>
<td>10</td>
<td>9.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence of Leaky Tank</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>9</td>
<td>10.3</td>
<td>-0.66</td>
<td>0.51</td>
</tr>
<tr>
<td>No</td>
<td>9</td>
<td>8.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence of Spillage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>15</td>
<td>8.8</td>
<td>-1.2</td>
<td>0.21</td>
</tr>
<tr>
<td>No</td>
<td>3</td>
<td>13.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
6.2.10 Summary

After reaching a maximum concentration, the decline of chlorpyrifos levels with the applicators was found to follow first-order kinetics per the equation,

\[
\ln \text{ADD} = -0.327 \text{Time} + 2 
\quad (R^2 0.99, \ p < 0.01)
\]

The first-order elimination half-life \(t_{1/2}\) of chlorpyrifos was therefore calculated to be about 50 hours. This suggests that the level of chlorpyrifos found with the applicators would be expected to return to background levels about 10 days after exposure (i.e. 5 half-lives).

Prior to the spray event, the levels of absorbed chlorpyrifos \(\text{LADD}_B\) of the applicators ranged from 0.05 to 2 µg/kg/day, with a median of 0.2 µg/kg/day. Following a spray event, the absorbed dose of chlorpyrifos \(\text{ADD}_A\) increased about 30-fold, ranging from 0.7 to 74 µg/kg/day, with a median of 6 µg/kg/day.

A statistical evaluation conducted showed that, the quantity of chlorpyrifos formulation applied, spraying duration, and the number of spray tanks applied, positively correlated with the levels of chlorpyrifos exposure from occupational application \(p < 0.05\). Therefore, to reduce exposure among applicators, interventions may be targeted at reducing the quantity of insecticide applied, duration of spraying, and the number of spray tanks applied.
6.3 Comparative Evaluation of Chlorpyrifos Exposure Estimates from Dermal Dosimetry and Urinary TCP Methods

6.3.1 Introduction

The conceptual framework of this research, based on the four-step health risk assessment framework of the United States’ National Research Council (USEPA, 2000; NRC, 2009), is shown in Figure 4.1 of Section 4.2 and repeated in this Section as Figure 6.9. The figure illustrates how the chapters and sections of the research fit into the conceptual framework. The main objectives of the overall research were to:

1. Identify hazardous pesticides and practices associated with the use of pesticides among applicators;
2. Assess the levels of chlorpyrifos exposure among applicators;
3. Evaluate the patterns of dermal exposure to chlorpyrifos among applicators;
4. Review the dose-response relationship of chlorpyrifos exposure and adverse effects;
5. Characterize the risks of adverse health effects due to chlorpyrifos exposure among applicators;

In Section 6.1 of this research, the levels of dermal exposure to chlorpyrifos with the applicators were assessed using the whole-body dosimetry method. The study focused on the dermal route because it has been identified as the major pathway by which pesticide applicators are exposed (Dowling and Seiber, 2002; Damalas and
Eleftherohorinos, 2011; Fenske et al., 2012). In fact, a study involving chlorpyrifos exposure among agricultural pesticide applicators identified the dermal route as accounting for about 94-96% of the total exposure (Fenske et al., 2012). Subsequent to the research described in Section 6.1, the overall levels of chlorpyrifos exposure with the rice farmers in this research were assessed based on urinary TCP method (Section 6.2), for a separate but similar exposure event as that for the dermal dosimetry method.

The objective of Section 6.3 is to compare the chlorpyrifos exposure estimates from the dermal dosimetry (Section 6.1) and urinary TCP (Section 6.2) methods.
Figure 6.9: The Section on Comparative Evaluation of Chlorpyrifos Exposure Estimates from Dermal Dosimetry and Urinary TCP Methods (highlighted with blue colour in the overall research framework) (see Figure 4.1 in Section 4.2)
6.3.2 Field Factors during the Dermal Dosimetry and Urinary TCP Assessments

In all, 24 applicators participated in the dermal dosimetry assessment, whereas 21 applicators participated in the urinary TCP assessment. However, the results of applicators (n = 16) who were involved in both the dermal dosimetry and the urinary TCP assessments were analysed in the current study.

Since the dermal dosimetry and urinary TCP assessments were undertaken during separate exposure events, differences in the field factors of the events could impact on the exposure dose estimates. To investigate this, the non-parametric Wilcoxon signed ranks test was employed to test for differences in medians of non-normally distributed continuous variables (quantity of insecticide applied, farm size and crop height) between the two assessments. A normally distributed continuous variable (spraying duration), on the other hand, was investigated using the parametric paired samples t-test on the means. For categorical variables (use of PPE, type of shirt, type of trouser, occurrences of leaky spray tank and insecticide spillage), the non-parametric McNemar test was used to test for differences in proportions.

The field factors recorded during the dermal and urinary TCP assessments are shown in Table 6.13. Also shown are the p-values of the statistical tests carried out to investigate differences in the field factors between the two exposure assessments (from Tables 6.1 and 6.5). Out of the nine field factors investigated, only two factors (farm size and spraying duration) differed significantly between the dermal dosimetry and urinary TCP assessments (0.4 ha and 0.6 ha; 53 min and 79 min, respectively; p < 0.05). It may therefore be assumed that the field factors of the dermal and biomonitoring assessments
were similar, especially, when the quantities of insecticide formulation applied during the two assessments were not statistically different (156 mL and 162 mL, respectively; p > 0.05). Compared to other field factors, quantity of pesticide applied has consistently been identified as a significant determinant of exposure among applicators (Aponso, 2002; Marquart et al., 2003; Bakke et al., 2009; Hines et al., 2011; Phung et al., 2012a; Atabila et al., 2017).

Table 6.11: Field Factors and p-values for Test of Difference in Variables between Dermal Dosimetry and Urinary TCP Methods (n=16).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Dermal Dosimetry Method</th>
<th>Urinary TCP Method</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantity of Insecticide Formulation Applied (median, mL)</td>
<td>156</td>
<td>162</td>
<td>0.43a</td>
</tr>
<tr>
<td>Farm Size (median, ha)</td>
<td>0.4</td>
<td>0.6</td>
<td>0.04a</td>
</tr>
<tr>
<td>Crop Height (median, cm)</td>
<td>43</td>
<td>38</td>
<td>0.5a</td>
</tr>
<tr>
<td>Spraying Duration (mean, min)</td>
<td>53</td>
<td>79</td>
<td>0.04b</td>
</tr>
<tr>
<td>Used PPE (%)</td>
<td>6</td>
<td>13</td>
<td>1c</td>
</tr>
<tr>
<td>Wore Short Sleeve Shirt (%)</td>
<td>63</td>
<td>50</td>
<td>0.7c</td>
</tr>
<tr>
<td>Wore long trousers (%)</td>
<td>100</td>
<td>94</td>
<td>1c</td>
</tr>
<tr>
<td>Occurrence of Leaky Spray Tank (%)</td>
<td>50</td>
<td>50</td>
<td>1c</td>
</tr>
<tr>
<td>Occurrence of Spillage (%)</td>
<td>81</td>
<td>81</td>
<td>1c</td>
</tr>
</tbody>
</table>

a, Wilcoxon signed ranks test; b, paired samples t-test; c, McNemar test
6.3.3 Absorbed Daily Dose of Chlorpyrifos Estimated from the Dermal Dosimetry Method (ADD<sub>DEM</sub>) and Urinary TCP Method (ADD<sub>TCP</sub>)

Shown in Table 6.14 are the descriptive statistics of the Absorbed Daily Dose (ADD) estimates of chlorpyrifos from the dermal dosimetry method (ADD<sub>DEM</sub>) and the urinary TCP method (ADD<sub>TCP</sub>). ADD<sub>DEM</sub> ranged from 5 to 29 µg/kg/day, with a median and a mean of 16 µg/kg/day. For ADD<sub>TCP</sub>, the dose estimate ranged from 1 to 71 µg/kg/day, with a median of 5 µg/kg/day and mean of 15 µg/kg/day. Although the median ADD<sub>DEM</sub> (16 µg/kg/day) was higher than that for ADD<sub>TCP</sub> (5 µg/kg/day), the difference was not statistically significant (p > 0.05) (Table 6.11). In addition, the means of ADD<sub>DEM</sub> (16 µg/kg/day) and ADD<sub>TCP</sub> (15 µg/kg/day) were similar. These suggest that, overall, the two methods yielded comparable results in terms of the central tendency measures.

Table 6.12: Absorbed Daily Dose of Chlorpyrifos Estimated from Dermal Dosimetry (ADD<sub>DEM</sub>) and Urinary TCP (ADD<sub>TCP</sub>) Methods (n = 16).

<table>
<thead>
<tr>
<th></th>
<th>Minimum</th>
<th>Median</th>
<th>Mean (±S.D)</th>
<th>Maximum</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADD&lt;sub&gt;DEM&lt;/sub&gt; (µg/kg/day)</td>
<td>5</td>
<td>16</td>
<td>16 (±7)</td>
<td>29</td>
<td>0.3a</td>
</tr>
<tr>
<td>ADD&lt;sub&gt;TCP&lt;/sub&gt; (µg/kg/day)</td>
<td>1</td>
<td>5</td>
<td>15 (±22)</td>
<td>71</td>
<td></td>
</tr>
</tbody>
</table>

a. Wilcoxon signed ranks test of difference of the median values
The CPD plots of ADD$_{DEM}$ and ADD$_{TCP}$ are shown in Figure 6.10. The linear regression line of the plot for ADD$_{DEM}$ and ADD$_{TCP}$ are respectively represented by the following equations:

\[
CP\% = 55\log(ADD_{DEM}) - 98 \quad (R^2 = 0.91, p < 0.01) \quad \text{Equation 6.8}
\]

\[
CP\% = 20\log(ADD_{TCP}) + 14 \quad (R^2 = 0.96, p < 0.001) \quad \text{Equation 6.9}
\]

The slope of the linear regression line of the plot for ADD$_{TCP}$ was less steep (20) compared to that of the plot for ADD$_{DEM}$ (55). These trends reflect the wide range (1 to 71 µg/kg/day) of ADD$_{TCP}$ values and the short range (5 to 29 µg/kg/day) of ADD$_{DEM}$ values (Table 6.11).

Figure 6.10 shows that ADD$_{DEM}$ values were generally higher than those for ADD$_{TCP}$ below the 75th percentile. Conversely, ADD$_{DEM}$ values were less than those for ADD$_{TCP}$ above the 75th percentile. If the exposure dose estimate from urinary TCP method is accepted as the most valid then, these findings suggest that dermal dosimetry method may over-estimate exposure dose at lower percentiles and under-estimate the dose at higher percentiles.

To further investigate the observed trend above, within the individual applicators, Absorbed Unit Exposure (AUE, %) values of both the dermal dosimetry and urinary TCP assessments for each applicator were calculated and compared. AUE values were calculated as a ratio of the mass of estimated absorbed chlorpyrifos to the mass of
chlorpyrifos applied, multiplied by 100. Thus, high absorbed chlorpyrifos corresponds to high AUE value. Plots of the AUE values are shown in Figure 6.11. With valid estimate of absorbed chlorpyrifos with the dermal dosimetry method, the resulting AUE values (AUE$_{DEM}$) and those from the urinary TCP method (AUE$_{TCP}$) for each applicator can be expected to be similar. However, Figure 6.11 shows that AUE$_{DEM}$ values were higher than AUE$_{TCP}$ for applicators A to L (“low exposure” group), reflecting Figure 6.8 with exposure below the 75$^{th}$ percentile. On the contrary, the reverse of this trend was true for applicators N to P (“high exposure” group), reflecting Figure 6.8 with exposure above the 75$^{th}$ percentile. These findings reinforce the observed trend from the CPD plots of ADD$_{DEM}$ and ADD$_{TCP}$ in Figure 6.10.

![Figure 6.10: Cumulative Probability Distribution (CPD) Plots of Absorbed Daily Dose of Chlorpyrifos Estimated from Dermal Dosimetry (ADD$_{DEM}$) and Urinary TCP (ADD$_{TCP}$) Methods (n = 16).](image)
Figure 6.11: Plots of Chlorpyrifos Absorbed Unit Exposure Values from Dermal Dosimetry (AUE\textsubscript{DEM}) and Urinary TCP (AUE\textsubscript{TCP}) Methods (n = 16).

The above findings also suggest that the dermal dosimetry was less able to account for variabilities in absorbed doses between applicators. This is mainly because the approach assumes that a fixed proportion (4.3\%) of the quantity of insecticide reaching the skin of applicators are absorbed, as demonstrated in the study by Meuling \textit{et al.} (2005) (see Section 4.6.7). On the contrary, urinary TCP assessment could account for variations in exposure doses between the applicators. Apart from the quantity of pesticide exposure on the skin, other differences between the applicators may contribute to variations in absorbed dose. These include the anatomical site of exposure, skin integrity, skin hydration, age and metabolic rates of the applicators (Holmgaard and Nielsen, 2009.).
6.3.4 Summary

Overall, the dermal dosimetry and urinary TCP methods for estimation chlorpyrifos exposure produced similar estimates, based on the means. However, exposure estimates from the urinary TCP method showed more variation than those from the dermal dosimetry method. Using the exposure estimate from the urinary TCP method as the reference, the dermal dosimetry method appeared to over-estimate exposure doses below the 75th percentile and under-estimate the doses above the 75th percentile.

Nevertheless, the dermal dosimetry method is a valuable approach for providing preliminary information regarding the typical initial levels of pesticide exposure among applicators. The urinary TCP method, which is usually associated with financial and technical challenges, may be used to identify the specific variations in exposure of individuals in a population. Moreover, the dermal dosimetry method may be used to identify the patterns of pesticide exposure on the anatomical regions of applicators as demonstrated in Section 6.1.4. This information is in turn, useful for identifying appropriate PPE for reducing pesticide exposure.
CHAPTER 7

CHLORPYRIFOS DOSE-RESPONSE AND TOXICANT SENSITIVITY DISTRIBUTION (TSD) ASSESSMENT

7.1 Introduction

The conceptual framework of this research, based on the four-step health risk assessment framework of the United States’ National Research Council (USEPA, 2000; NRC, 2009), is shown in Figure 4.1 of Section 4.2 and repeated in this chapter as Figure 7.1. The figure illustrates how the chapters and sections of the research fit into the conceptual framework. The objectives of the overall research were to:

1. Identify hazardous pesticides and practices associated with the use of pesticides among applicators;
2. Assess the levels of chlorpyrifos exposure among applicators;
3. Evaluate the patterns of dermal exposure to chlorpyrifos among applicators;
4. Review the dose-response relationship of chlorpyrifos exposure and adverse effects;
5. Characterize the risks of adverse health effects due to chlorpyrifos exposure among applicators;

Chapter 6 reports on the levels of chlorpyrifos exposure among the applicators in the study through dermal exposure (Section 6.1) and overall exposure (Section 6.2) to address objectives 2 and 3 of the overall research.
The objective of Chapter 7, highlighted with purple colour in Figure 7.1, is to present the results and discussion of the review (Section 4.8) done to evaluate dose-response data used in establishing chlorpyrifos guideline values. Chapter 7 addresses objective 4 of the overall research. The review took into account chlorpyrifos guideline values derived with conventional methods as well as those derived using probabilistic techniques. The information obtained from Chapter 7 will be integrated with those from Sections 6.1 and 6.2 to characterize the risk of adverse health effects among the applicators in Chapter 8 of the research.
Figure 7.1: The Section on Chlorpyrifos Dose-Response and Toxicant Sensitivity Distribution (TSD) Assessment (highlighted with purple colour in the overall research framework) (see Figure 4.1 in Section 4.2)
7.2 Conventional Guideline Values for Health Risk Assessment with Chlorpyrifos

Guideline Values for evaluation of health risk of chemicals are usually developed based on a dose-response relationship of a toxicant. This relationship is a quantitative description of the association between observed adverse effects in humans or animals at various exposure doses of the toxicant (Connell, 2005). Guideline values are levels of a toxicant below which no adverse effects are expected but above which such effects are expected. Usually, guideline values are developed through laboratory measurement of the No Observed Adverse Effect Level (NOAEL) or Lowest Observed Adverse Effect Level (LOAEL) with surrogate animals. Since the former constitutes the more sensitive and appropriate endpoint, it is generally employed, provided the necessary data are available. To account for variability and uncertainties, appropriate safety factors are then applied to the NOAEL or LOAEL to obtain Guideline Values which are used in health risk assessment and to help regulate human exposure to toxicants (Sections 3.3).

The human health effects of chlorpyrifos have been extensively studied, with various Guideline Values obtained by different countries and agencies based on different biological characteristics. The acute and chronic guideline values set by some regulatory agencies are shown in Table 7.1. The most widely accepted endpoint for determining a NOAEL for chlorpyrifos and other organophosphate insecticides in general, is cholinesterase inhibition, utilizing plasma butyrylcholinesterase, erythrocyte acetylcholinesterase and brain acetylcholinesterase (Zhao et al., 2006).
Using a NOAEL of 1,000 µg/kg/day from a single-dose human study on inhibition of erythrocyte acetylcholinesterase and a safety factor of 10, the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) in 1999 established an acute guideline value of 100 µg/kg/day for chlorpyrifos (WHO, 2009c). With a NOAEL of 30 µg/kg/day from a human study on cholinesterase inhibition and a safety factor of 10, the USEPA initially established an acute guideline value of 3 µg/kg/day for chlorpyrifos (ATSDR, 2006). However, the USEPA later re-evaluated the guideline values of chlorpyrifos based on new scientific data and ethical concerns. The new acute guideline value was set at 5 µg/kg/day using a NOAEL of 500 µg/kg/day from rat study on plasma butyrylcholinesterase and a safety factor of 100 (USEPA, 2000; ATSDR, 2006). In Australia, the National Registration Authority (NRA) for Agricultural and Veterinary Chemicals, now called the Australian Pesticides and Veterinary Medicines Authority (APVMA), has set the acute guideline value for chlorpyrifos at 10 µg/kg/day. This was based on a NOAEL of 100 µg/kg/day from 28-day human study on plasma butyrylcholinesterase, and a safety factor of 10 (NRA, 2000).
Table 7.1: Chlorpyrifos Guideline Values with NOAELs, Safety Factors and Endpoints Established by the Different Regulatory Agencies.

<table>
<thead>
<tr>
<th>Agency</th>
<th>Guideline Value (µg/kg/day)</th>
<th>NOAEL (µg/kg/day)</th>
<th>Safety Factor</th>
<th>Endpoint</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acute</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WHO</td>
<td>100</td>
<td>1,000</td>
<td>10</td>
<td>Inhibition of erythrocyte acetylcholinesterase in a single dose human study.</td>
<td>WHO, 2009b</td>
</tr>
<tr>
<td>USEPA</td>
<td>5</td>
<td>500</td>
<td>100</td>
<td>Inhibition of plasma butyrylcholinesterase in rats.</td>
<td>USEPA, 2000</td>
</tr>
<tr>
<td>APVMA</td>
<td>10</td>
<td>100</td>
<td>10</td>
<td>Inhibition of plasma butyrylcholinesterase in human study.</td>
<td>NRA, 2000</td>
</tr>
<tr>
<td></td>
<td>Chronic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WHO</td>
<td>10</td>
<td>100</td>
<td>10</td>
<td>Inhibition of erythrocyte acetylcholinesterase in a 9-day human study.</td>
<td>WHO, 2000</td>
</tr>
<tr>
<td>USEPA</td>
<td>0.3</td>
<td>30</td>
<td>100</td>
<td>Inhibition of plasma and erythrocyte cholinesterase inhibition in dogs and rats.</td>
<td>USEPA, 2000</td>
</tr>
<tr>
<td>APVMA</td>
<td>3</td>
<td>30</td>
<td>10</td>
<td>Inhibition of plasma butyrylcholinesterase in human study.</td>
<td>NRA, 2000</td>
</tr>
</tbody>
</table>

The chronic toxicity of chlorpyrifos was initially evaluated by the JMPR in 1972 which established chronic guideline value of 1.5 µg/kg/day. This was based on a NOAEL of 14 µg/kg/day from a one-month human study and a safety factor of 10. The chronic guideline value was reduced to 1 µg/kg/day by the JMPR in 1977 based on new toxicological data. However, the JMPR in 1982 reviewed the guideline value upwards to 10 µg/kg/day, based on a NOAEL of 100 µg/kg/day in a 9-day human study on erythrocyte acetylcholinesterase inhibition and safety factor of 10 (WHO, 2000). The USEPA calculated the chronic guideline value of chlorpyrifos to be 0.3 µg/kg/day, using a NOAEL of 30 µg/kg/day from dogs and rats study on plasma and erythrocyte cholinesterase inhibition, and a safety factor of 100. The APVMA (Australia) determined the chronic guideline value of chlorpyrifos to be 3 µg/kg/day, based on a NOAEL of 30 µg/kg/day from a 28-human study on butyrylcholinesterase inhibition and safety factor of 10.
With the guideline values reported, those established by the WHO have been highest, followed by those of APVMA, with those of the USEPA being the lowest. This is due to the use of erythrocyte cholinesterase inhibition by the WHO to set the guideline values, in contrast to the use of mainly plasma cholinesterase by the USEPA and APVMA (Table 7.1). Compared to plasma cholinesterase, erythrocyte cholinesterase inhibition is less sensitive to chlorpyrifos (Zhao et al., 2006; Eaton et al., 2008; APVMA, 2009). Also, whereas the WHO and APVMA applied a safety factor of 10 because of the use of human data to derive the NOAEL, the USEPA applied a safety factor of 100 due to the use of animal data.

There are several problems associated with the use of NOAEL and LOAEL values to derive guideline values. For instance, these approaches result in a single reference dose that is assumed to have no or minimum adverse effects. However, variability in sensitivities that may exist in a population are not expressed (WHO, 2009b). This variability in sensitivities may arise due to factors such as age, gender, race, and health status. Also, the use of different toxicological end-points and safety factors by different agencies and countries has resulted in different guideline values for chlorpyrifos. This inconsistency may complicate risk assessment efforts, particularly in developing countries who rely on guideline values set by international bodies and developed countries.
7.3 Chlorpyrifos Toxicant Sensitivity Distributions (TSDs)

In this research, the challenges associated with the use of the NOAEL and LOAEL approaches to derive guideline values as outlined above, was addressed through the use of probabilistic techniques to express the sensitivities of humans to adverse effects of chlorpyrifos. In Section 4.8.2, human epidemiological studies from the scientific literature reporting both adverse effects of chlorpyrifos and the corresponding exposure levels were collated. The exposure levels were converted to Absorbed Daily Dose (ADD) and Lifetime Absorbed Daily Dose (LADD) of chlorpyrifos for acute and chronic adverse effects, respectively. The calculated ADD and LADD data were then expressed as Cumulative Probability Distributions (CPDs) to derive the Toxicant Sensitivity Distributions (TSDs) for chlorpyrifos.

The majority of the studies reviewed were related to acute occupational exposure (Steenland et al., 2000; Dick et al., 2001; Albers et al., 2004; Albers et al., 2007; Garabrant et al., 2009; Farahat et al., 2011; Khan et al., 2014; Wang et al., 2016), whereas a small number were related to chronic background exposure (Berkowitz et al., 2004; Meeker et al., 2006; Meeker et al., 2008). Depending on the exposure scenario, the estimated doses from the studies were categorized as acute dose (TSD_{ACUTE} Dose) or chronic dose (TSD_{CHRONIC} Dose). For TSD_{ACUTE} doses, the corresponding TSD_{CHRONIC} doses were estimated using Equation 4.9 (Section 4.8.2). The TSD_{ACUTE} and TSD_{CHRONIC} doses are presented in Table 7.2.
Table 7.2: Acute and Chronic Toxicant Sensitivity Distribution (TSD) Doses of Chlorpyrifos from Human Epidemiological Studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Study Subjects</th>
<th>N</th>
<th>Reported Exposure Level</th>
<th>TSD\text{\text{ACUTE}} Dose* (μg/kg/day)</th>
<th>TSD\text{\text{CHRONIC}} Dose (μg/kg/day)</th>
<th>Reported Adverse Health Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steeland et al., 2000</td>
<td>Cross-sectional</td>
<td>Termiticide applicators</td>
<td>380</td>
<td>629.5 µg/L urine</td>
<td>36</td>
<td>11**</td>
<td>Poor performance in pegboard turning tests and postural sway tests. More symptoms of memory problems, emotional states, fatigue, and loss of muscle strength.</td>
</tr>
<tr>
<td>Dick et al., 2001</td>
<td>Cross-sectional</td>
<td>Termiticide applicators</td>
<td>158</td>
<td>200 µg/g creatinine</td>
<td>16</td>
<td>5**</td>
<td>Adverse effect on postural sway in the eyes closed and soft-surface conditions, suggesting a possible subclinical effect involving the proprioceptive and vestibular systems.</td>
</tr>
<tr>
<td>Albers et al., 2004</td>
<td>Longitudinal</td>
<td>Chlorpyrifos manufacturing workers</td>
<td>113</td>
<td>192.2 µg/g creatinine</td>
<td>16</td>
<td>6**</td>
<td>Depression of butyrylcholinesterase activity.</td>
</tr>
<tr>
<td>Albers et al., 2007</td>
<td>Longitudinal</td>
<td>Chlorpyrifos manufacturing workers</td>
<td>113</td>
<td>576–627 µg/day</td>
<td>17</td>
<td>6**</td>
<td>Adverse effects on peripheral nerve electrophysiology, which is suggestive of subclinical neuropathy.</td>
</tr>
<tr>
<td>Garabrant et al., 2009</td>
<td>Cross-sectional</td>
<td>Chemical manufacturing workers</td>
<td>113</td>
<td>&gt;110 µg/g creatine</td>
<td>5</td>
<td>2**</td>
<td>Depression of butyrylcholinesterase activity.</td>
</tr>
<tr>
<td>Farahat et al., 2011</td>
<td>Cross-sectional</td>
<td>Farm applicators</td>
<td>38</td>
<td>3,161 µg/g creatinine</td>
<td>181</td>
<td>3**</td>
<td>Depression of butyrylcholinesterase activity.</td>
</tr>
<tr>
<td>Wang et al., 2016</td>
<td>Cross-sectional</td>
<td>Adult farmers</td>
<td>35</td>
<td>3.70 µg/kgbw/day</td>
<td>4</td>
<td>0.6**</td>
<td>Increase in urinary 8-hydroxydeoxyguanosine (8-OHdG). An indication of potential oxidative damage to DNA.</td>
</tr>
<tr>
<td>Khan et al., 2014</td>
<td>Longitudinal</td>
<td>Adolescent farmers</td>
<td>95</td>
<td>137 µg/g creatinine</td>
<td>8</td>
<td>1**</td>
<td>Increase in self-reported neurological symptoms.</td>
</tr>
<tr>
<td>Berkowitz et al., 2004</td>
<td>Longitudinal</td>
<td>General population (mothers and infants)</td>
<td>404</td>
<td>11.5 µg/g creatinine</td>
<td>NA</td>
<td>0.5*</td>
<td>Detrimental effect on fetal neurodevelopment among mothers who exhibit low PON1 activity.</td>
</tr>
<tr>
<td>Meeker et al., 2006</td>
<td>Cross-sectional</td>
<td>General population (adult men)</td>
<td>301</td>
<td>1.83 µg/g creatinine</td>
<td>NA</td>
<td>2.6*</td>
<td>Altered thyroid function in human.</td>
</tr>
<tr>
<td>Meeker et al., 2008</td>
<td>Cross-sectional</td>
<td>General population (adult men)</td>
<td>322</td>
<td>2.59 µg/L urine</td>
<td>NA</td>
<td>2.6*</td>
<td>Reductions in estradiol levels.</td>
</tr>
<tr>
<td><strong>Mean ± SD</strong></td>
<td></td>
<td></td>
<td>35</td>
<td>± 60</td>
<td>3.1 ± 3.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The CPD plots of TSD_{ACUTE} and TSD_{CHRONIC} doses are shown in Figure 7.2. The linear regression lines using all data points of TSD_{ACUTE} and TSD_{CHRONIC} are respectively represented by the following equations:

\[
\text{CP (\%)} = 48\log (\text{TSD}_{\text{ACUTE}}) - 8 \quad (R^2 = 0.87, \ p < 0.01) \quad \text{Equation 7.1}
\]

\[
\text{CP (\%)} = 63\log (\text{TSD}_{\text{CHRONIC}}) + 25 \quad (R^2 = 0.96, \ p < 0.001) \quad \text{Equation 7.2}
\]

The dose at the 5^{th} percentile (CP_{5}) of TSD_{ACUTE} and TSD_{CHRONIC} were determined to be 2 and 0.5 µg/kg/day, respectively. The TSD dose at the 5^{th} percentile may be regarded as the lowest dose above which the most sensitive group of the population exhibits adverse effects (Connell, 2005). Usually, doses below the 5^{th} percentile are not considered to be reliable. However, in the present data set there were no data points below the 5^{th} percentile. Exposure doses above the TSD dose at the 5^{th} percentile would therefore constitute a risk of adverse effects, whereas exposure doses below the TSD dose at the 5^{th} percentile would not constitute risk of adverse effects and there have been no reports of adverse effects below this level. The doses at the 5^{th} percentiles of TSD_{ACUTE} (2 µg/kg/day) and TSD_{CHRONIC} (0.5 µg/kg/day) obtained in the present study are similar to those (3 µg/kg/day and 0.5 µg/kg/day, respectively) obtained in the study by Phung et al. (2015).
Figure 7.2: Cumulative Probability Distribution (CPD) Plot of Acute and Chronic Toxicant Sensitivity Distribution Doses of Chlorpyrifos from Human Epidemiological Studies.

7.4 Summary

Guideline values established for evaluating health risks of chlorpyrifos exposure in human populations are variable, depending on the toxicological end points applied. The chronic guideline values derived with conventional methods were 0.3, 3 and 10 µg/kg/day, according to the WHO, USEPA and APVMA, respectively. With acute guidelines, the values established by the WHO, USEPA and APVMA were 100, 10 and 5 µg/kg/day, respectively. Using the TSD method, chronic and acute guideline value of 0.5 and 2 µg/kg/day, respectively were obtained. These guideline values have been applied to characterize the risk of adverse effects among the applicators in Chapter 8 of the research.
CHAPTER 8

RISK CHARACTERIZATION OF CHLORPYRIFOS EXPOSURE WITH APPLICATORS ON RICE FARMS IN GHANA

8.1 Risk Characterization of Chlorpyrifos Exposure Estimated from Dermal Dosimetry with the Applicators

8.1.1 Introduction

The conceptual framework of this research, based on the four-step health risk assessment framework of the United States’ National Research Council (USEPA, 2000; NRC, 2009), is shown in Figure 4.1 of Section 4.2 and repeated in this section as Figure 8.1. The figure illustrates how the chapters and sections of the research fit into the conceptual framework. The main objectives of the overall research were to:

1. Identify hazardous pesticides and practices associated with the use of pesticides among applicators;
2. Assess the levels of chlorpyrifos exposure among applicators;
3. Evaluate the patterns of dermal exposure to chlorpyrifos among applicators;
4. Review the dose-response relationship of chlorpyrifos exposure and adverse effects;
5. Characterize the risks of adverse health effects due to chlorpyrifos exposure among applicators;
Section 6.1 of the thesis described the levels, patterns and determinants of Total Dermal Exposure (TDE) to chlorpyrifos with the applicators, using the whole body dermal dosimetry method. Based on the TDE values (Table 6.4, Section 6.1.6), Absorbed Daily Dose (ADD) and Lifetime Average Daily Dose (LADD) of chlorpyrifos due to dermal exposure were estimated. The ADD values of the applicators ranged from 4.8 to 28.5µg/kg/day, with a mean (±S. D) of 16 µg/kg/day (±6.0). With LADD, the values ranged from 0.08 to 0.47µg/kg/day, with a mean (±S. D) of 0.3 (± 0.1) µg/kg/day.

The objective of Section 8.1, highlighted with red colour in Figure 8.1, is to present the results and discussion of the health risk characterization study (Section 4.9) conducted using the applicator exposure data outlined above. Section 8.1 addresses objective 5 of the overall research. To meet this objective, acute and chronic health risks were evaluated with the Hazard Quotient (HQ) technique, using conventional guideline values promulgated by regulatory agencies (Table 7.1, Section 7.2.)
Figure 8.1: The Section on Risk Characterization with Exposure Estimate from Dermal Dosimetry (highlighted with red colour in the overall research framework) (see Figure 4.1 in Section 4.2).
8.1.2 Cumulative Probability Distribution Plots of ADD\(_D\) and LADD\(_D\) of Chlorpyrifos with the Applicators from Dermal Exposure

The CPD plots of ADD\(_D\) and LADD\(_D\) of the applicators were constructed from data in Table 6.4 and are presented in Figures 8.2 and 8.3, respectively. The CPD plots provide the relative frequencies of all chlorpyrifos exposure doses with the applicators, allowing the determination of the probability of occurrence of the doses. The linear part of the plots for both ADD\(_D\) and LADD\(_D\) were all determined to lie between 8% and 92% of the CPD, based on the R\(^2\) values. The corresponding equations of the linear regression lines fitted to the CPD plot of ADD\(_D\) and LADD\(_D\), respectively were:

\[
\text{CP} (\%) = 175\log (\text{ADD}_D) - 157 \quad (R^2 = 0.92, \ p < 0.001) \quad \text{Equation 8.1}
\]

\[
\text{CP} (\%) = 154\log (\text{LADD}_D) + 141 \quad (R^2 = 0.95, \ p < 0.001) \quad \text{Equation 8.2}
\]

where CP is the exposure Cumulative Probability, ADD\(_D\), the dermal Absorbed Daily Dose, and LADD\(_D\), the dermal Lifetime Average Daily Dose.
Figure 8.2: Cumulative Probability Distribution (CPD) Plot of ADD$_D$ Levels of Chlorpyrifos from Dermal Exposure with Applicators on Rice Farms in Ghana.

Figure 8.3: Cumulative Probability Distribution Plot (CPD) of LADD$_D$ Levels of Chlorpyrifos from Dermal Exposure with Applicators on Rice Farms in Ghana.
In this study, exposure doses at the 50th percentile (CP₅₀) and 95th percentile (CP₉₅) were considered the most useful to characterise the risk of adverse health effects. CP₅₀ is usually used to describe exposure among the median exposed group, while CP₉₅ is used to describe exposure among the highly-exposed group. Exposure control measures that would aim to protect the highly-exposed group would also give protection to most of the rest of the population. The highly-exposed group may therefore be regarded as the main group of concern for health risk assessment and management. Figure 8.2 shows that CP₅₀ for ADD_D was 15 µg/kg/day, which was close to the mean value of 16 µg/kg/day calculated previously in Section 6.1.6 (Table 6.4). Similarly, Figure 8.3 indicates that CP₅₀ for LADD_D (0.3 µg/kg/day) was the same as the mean obtained in Section 6.1.6. These suggest that the distributions of both ADD_D and LADD_D were not skewed and were therefore close to a normal distribution.

8.1.3 The Hazard Quotient Technique

Conventionally, the Hazard Quotient (HQ) for non-carcinogenic toxicants is obtained by identifying a single point estimate of exposure that is most representative of a population and dividing it by the appropriate guideline value of the toxicant (USEPA, 1992). HQ values less than or equal to unity imply minimal or no risk of adverse health effects, whereas, HQ values above unity constitute risks of adverse health effects due to exposure to the toxicant.

The HQ technique of characterising health risks of environmental and occupational toxicants is simple to calculate and to understand. The technique, however, cannot
usually account for the variability of exposure and sensitivity among a population. A strategy to partly address this weakness is to calculate HQ at various percentiles of exposure (Cao et al., 2010; Phung et al., 2012a; Marasinghe et al., 2014; Edokpolo et al., 2015; Sadler et al., 2016). In this study, HQ was calculated for exposures at CP_{50} (HQ_{50}) and CP_{95} (HQ_{95}), which represents the risk among the median exposed group and the 5% highly-exposed group, respectively. The risk levels among these two groups are regarded the most important in terms of managing toxicant exposure and adverse health effects in a population.

8.1.4 Hazard Quotients (HQs) due to Acute Dermal Exposure to Chlorpyrifos

The Hazard Quotient (HQ) technique was applied using different guideline values to quantitatively describe the risk of adverse health effects due to chlorpyrifos exposure with the applicators studied. With the HQ technique, HQ values less or equal to unity are generally believed to be associated with a low probability for the occurrence of adverse health effects, whereas HQ values more than unity may be associated with high probability for the occurrence of adverse health effects.

The HQ values corresponding to CP_{50} (HQ_{50}) and CP_{95} (HQ_{95}) for ADD$_D$ are presented in Table 8.1. The HQ_{50} values for ADD$_D$ (3, 1.5, and 5) obtained with the guideline values derived by the USEPA, APVMA, and Phung et al. (2015), respectively, were above unity. But HQ_{50} was less than unity with the guideline value set by the WHO (HQ_{50} = 0.2). Similarly, HQ_{95} for ADD$_D$ obtained with the guideline value by USEPA, APVMA, and Phung et al. (2015) were all above unity (HQ_{95} = 5.4, 2.7, and 9
respectively). However, HQ\textsubscript{95} with the WHO’s guideline value was less than unity (HQ\textsubscript{95} = 0.3). The HQ\textsubscript{50} values obtained for ADD\textsubscript{D} with the guideline values by the USEPA, APVMA, and Phung et al. (2015) suggest that there was a high chance for occurrence of adverse health effects to occur due to acute chlorpyrifos exposure, both with the median exposed group as well as the highly-exposed group of the applicators studied (HQ\textsubscript{50} and HQ\textsubscript{95} > 1). On the contrary, the HQ values calculated with the WHO’s guideline value indicate that there was low chance for adverse health effects to occur due to acute chlorpyrifos exposure with both the median exposed group and the highly-exposed group (HQ\textsubscript{50} and HQ\textsubscript{95} < 1).

The TSD evaluation with chlorpyrifos conducted by Phung et al. (2015), using human epidemiological studies, suggests the acute adverse health effects that could occur with the median exposed and 5% highly-exposed groups, may include Acetylcholinesterase (AChE) and Butyrylcholinesterase (BuChE) inhibition; sensory and motor effects; and subclinical neuropathy. On the other hand, adverse effects on human health are not revealed with the HQ calculated using WHO, USEPA and APVMA values.
Table 8.1: Hazard Quotients (HQ<sub>50</sub> and HQ<sub>95</sub>) for ADD<sub>D</sub> Levels of Chlorpyrifos from Dermal Exposure with Applicators on Rice Farms in Ghana

<table>
<thead>
<tr>
<th>Guideline</th>
<th>ADD&lt;sub&gt;D&lt;/sub&gt; (µg/kg/day)</th>
<th>CP&lt;sub&gt;50&lt;/sub&gt;</th>
<th>CP&lt;sub&gt;95&lt;/sub&gt;</th>
<th>Hazard Quotient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>Value (µg/kg/day)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WHO (2009)</td>
<td>100</td>
<td>15</td>
<td>27</td>
<td>0.2</td>
</tr>
<tr>
<td>USEPA (2000)</td>
<td>5</td>
<td>15</td>
<td>27</td>
<td>3.0</td>
</tr>
<tr>
<td>APVMA (2009)</td>
<td>10</td>
<td>15</td>
<td>27</td>
<td>1.5</td>
</tr>
<tr>
<td>Phung et al (2015)</td>
<td>3</td>
<td>15</td>
<td>27</td>
<td>5.0</td>
</tr>
</tbody>
</table>

(HQ values > 1 are coloured red)

8.1.5 Hazard Quotients (HQs) due to Chronic Dermal Exposure to Chlorpyrifos

The HQ<sub>50</sub> and HQ<sub>95</sub> values for LADD<sub>D</sub> are presented in Table 8.2. The HQ<sub>50</sub> values obtained using the guideline values set by the WHO, USEPA, APVMA, and Phung et al. (2015) were all less or equal to unity (HQ<sub>50</sub> = 0.03, 1.0, 0.1, and 0.6, respectively) (Table 7.2). Likewise, the HQ<sub>95</sub> values obtained with the guideline values of the WHO and APVMA were less than unity (HQ<sub>95</sub> = 0.1 and 0.2, respectively). However, the HQ<sub>95</sub> calculated with USEPA’s and Phung et al.’s guideline values were more than unity (HQ<sub>95</sub> = 2.0 and 1.2, respectively).

With the HQ<sub>50</sub> values obtained for LADD<sub>D</sub>, all the guideline values suggest that there was low chance for adverse health effects to occur due to chronic exposure to chlorpyrifos with the median exposed group of the applicators studied (HQ<sub>50</sub> < 1). Similarly, the guideline values from the WHO and APVMA suggest a low chance of adverse health effects among the highly-exposed group, regarding chronic exposure to chlorpyrifos (HQ<sub>95</sub> < 1). In contrast, the guideline values by the USEPA and Phung et
al. (2015) suggest a high chance for adverse health effects among the highly-exposed group due to chronic chlorpyrifos exposure (HQ95 > 1). The possible adverse health effects that may be experienced by the 5% highly-exposed group (CP95) of the applicators due to chronic exposure to chlorpyrifos may include DNA damage in sperm, decreased testosterone and thyroid hormone free T4 levels; and increased Thyroid Stimulating Hormones (TSH) (Phung et al., 2015).

Table 8.2: Hazard Quotients (HQ50 and HQ95) for LADDp Levels of Chlorpyrifos from Dermal Exposure with Applicators on Rice Farms in Ghana

<table>
<thead>
<tr>
<th>Guideline</th>
<th>LADDp(µg/kg/day)</th>
<th>Hazard Quotient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Value(µg/kg/day)</td>
<td>CP50</td>
</tr>
<tr>
<td>WHO (2009)</td>
<td>10.0</td>
<td>0.3</td>
</tr>
<tr>
<td>USEPA (2000)</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>APVMA (2009)</td>
<td>3.0</td>
<td>0.3</td>
</tr>
<tr>
<td>Phung et al (2015)</td>
<td>0.5</td>
<td>0.3</td>
</tr>
</tbody>
</table>

(HQ values > 1 are coloured red)

8.1.6 Variations Resulting from Different Guideline Values

The variations in both the acute and chronic guideline values for chlorpyrifos have resulted in different HQ values for both CP50 and CP95 (Tables 8.1 and 8.2). The differences in the guideline values are a result of the different approaches and toxicological endpoints that were applied to derive the values, as explained previously by Phung et al. (2013). The guideline values set by the WHO, USEPA, and APVMA were all based on the No Observable Adverse Effect Level (NOAEL) approach. In this
approach experiments were conducted with appropriate animal models to identify toxicological endpoints and the endpoint with the lowest NOAEL was selected and relevant safety factors applied to derive the guideline values (Connell, 2005). The guideline values derived by Phung et al., (2015) on the other hand, were based on evaluation using data from human epidemiological studies. It is suggested that these guidelines are more directly applicable to humans without the need for safety factors, which is subjective and introduce uncertainties in the risk characterization process (Wu et al., 2008).

Countries that do not have their own national guideline values, such as Ghana, usually rely on the guideline values derived by international and other organisations, for health risk assessment studies. Therefore, the wide variation in the guideline values of toxicants, such as chlorpyrifos, complicates health risk assessment efforts in such countries. Consequently, a burden is placed on the authorities responsible for human health risk assessment in those countries to decide on the most appropriate guideline value that is suitable to their context. To select a suitable guideline value, consideration may be given to guideline values that would provide the maximum level of protection to the general population. It should also be practical so that facilities and personnel are available to enforce the guideline selected. Guideline values that are lower may be regarded as the most protective of public health. However, enforcement of such guideline values could be difficult in many developing countries. This is largely because of poor safety knowledge, practices and systems with farmers, usually leading to high levels of exposure. Industries and livelihoods may therefore be crippled if impractical guideline values are strictly applied. Perhaps, a more pragmatic approach would be to adopt a more practical guideline value (that may be higher than others) and periodically
review the adopted guideline value, aiming for a more protective one as efforts are made to improve the safety situation.

8.1.7 Summary

The dermal exposure dose of chlorpyrifos at the 50\textsuperscript{th} and 95\textsuperscript{th} percentiles of ADD\textsubscript{D} were 15 µg/kg/day and 27µg/kg/day, respectively. Apart from the acute guideline value set by the WHO (2009), the remaining acute guidelines used in the present study (USEPA, 2009; APVMA, 2009; and Phung \textit{et al.}, 2015), indicated that applicators represented by the median (CP\textsubscript{50}) and the 5\% highly (CP\textsubscript{95}) exposed groups were at high risk of adverse health effects due to acute dermal chlorpyrifos exposure (HQ\textsubscript{50} > 1 and HQ\textsubscript{95} > 1). With the LADD\textsubscript{D}, the exposure dose at the 50\textsuperscript{th} and 95\textsuperscript{th} percentiles were 0.3 µg/kg/day and 0.6 µg/kg/day, respectively. None of the chronic guideline values used to evaluate LADD\textsubscript{D} in the present study suggested risk of adverse health among the median exposed group (HQ\textsubscript{50} < 1). Similarly, chronic guideline values of the WHO and APVMA did not suggest risk of adverse health effect among the highly-exposed group (HQ\textsubscript{95} < 1). However, the guideline values of the USEPA and Phung \textit{et al.} (2015) suggested there may be adverse health effects (HQ\textsubscript{95} > 1).

In terms of acute health effects, there is strong evidence from this study that both the median and 5\% highly-exposed applicator groups could suffer adverse effects from chlorpyrifos exposure. With chronic health effects, there are evidence that the 5\% highly-exposed applicator group may suffer adversely. There was however, no evidence that the median exposed-group would suffer chronic adverse effects.
8.2 Risk Characterization of Overall Chlorpyrifos Exposure Estimated from Urinary TCP with the Applicators

8.2.1 Introduction

The conceptual framework of this research, based on the four-step health risk assessment framework of the United States’ National Research Council (USEPA, 2000; NRC, 2009), is shown in Figure 4.1 of Section 4.2 and repeated in this section as Figure 8.4. The figure illustrates how the chapters and sections of the research fit into the conceptual framework. The main objectives of the overall research were to:

1. Identify hazardous pesticides and practices associated with the use of pesticides among applicators;
2. Assess the levels of chlorpyrifos exposure among applicators;
3. Evaluate the patterns of dermal exposure to chlorpyrifos among applicators;
4. Review the dose-response relationship of chlorpyrifos exposure and adverse effects;
5. Characterize the risks of adverse health effects due to chlorpyrifos exposure among applicators;

Section 6.2 of the thesis described the levels of exposure to chlorpyrifos with the applicators, based on urinary 3, 5, 6-trichloro-2-pyridinol (TCP). The equivalent Lifetime Average Daily Dose (LADD) and Absorbed Daily Dose (ADD) of chlorpyrifos were estimated from the TCP levels. The median Lifetime Average Daily Dose (LADD) of chlorpyrifos from background exposure was 0.2 µg/kg/day, with a mean (±S. D) of 0.3 (± 0.4) µg/kg/day (Table 6.10, Section 6.2.7). With the Absorbed
Daily Dose (ADDₐ) of chlorpyrifos from occupational application, the median was 5.6 µg/kg/day, with a mean (±S. D) of 19 (± 24) µg/kg/day. The Lifetime Average Daily Dose (LADDₐ) of chlorpyrifos from occupational application had a median value of 0.1 µg/kg/day with a mean (±S. D) of 0.3 (± 0.3) µg/kg/day.

The objective of Section 8.2, highlighted with red colour in Figure 8.4, is to present the results and discussion of the health risk characterization study (Section 4.9) conducted using the chlorpyrifos exposure data reported above from Section 6.2. To meet this objective, acute and chronic health risks were evaluated with both the HQ and probabilistic (Monte Carlo Simulation and Overall Risk Probability) techniques, using chlorpyrifos guideline values and Toxicant Sensitivity Distribution (TSD), respectively. Conventional guideline values promulgated by regulatory agencies were used, but in addition, guideline values set using probabilistic techniques (Section 7.3) were applied.
Figure 8.4: The Section on Risk Characterization with Chlorpyrifos Exposure Estimates from Urinary TCP (highlighted with red colour in the overall research framework) (see Figure 4.1 in Section 4.2).
8.2.2 Cumulative Probability Distribution (CPD) of Acute and Chronic Exposure Doses of Chlorpyrifos

Generally, exposures to chlorpyrifos occur from background sources (e.g. food, water and air) in the environment, as well as from occupational application. Evaluation of chronic health risk due to chlorpyrifos exposure in this study was based on chronic exposure under three scenarios. These were:

(1) Lifetime Average Daily Dose of chlorpyrifos from background exposure (LADD\text{B});

(2) Lifetime Average Daily Dose of chlorpyrifos from application exposure (LADD\text{A}); and

(3) Total Lifetime Average Daily Dose of chlorpyrifos from both background and application exposures (LADD\text{T}) (i.e. LADD\text{T} = LADD\text{B} + LADD\text{A}).

For acute health risks, the evaluation was based on acute exposure under two scenarios. These were:

(1) Absorbed Daily Dose of chlorpyrifos from application exposure (ADD\text{A});

and

(2) Total Absorbed Daily Dose of chlorpyrifos from both background and application exposures (ADD\text{T}) (i.e. ADD\text{T} = LADD\text{B} + ADD\text{A}).

The CPD plots of LADD\text{B}, LADD\text{A}, and LADD\text{T} obtained with the data from Table 6.10 (Section 6.2.7) are presented in Figure 8.5. The linear part of the CPD plots of the levels of environmental and occupational toxicants are generally found between 20th
percentile or below (lower bound) and 80\textsuperscript{th} percentile or above (upper bound) of the
CPD plot (Edokpolo et al., 2015; Sadler et al., 2016). The linear parts of the plots were
all determined to lie between 11\% – 89\% of the CPD plots. The equations of the
corresponding regression lines of LADD\textsubscript{B}, LADD\textsubscript{A} and LADD\textsubscript{T} were respectively:

\begin{align*}
CP &= 113\log\text{LADD}_B + 130 \quad (R^2 = 0.94, \ p < 0.001) & \text{Equation 8.3} \\
CP &= 44\log\text{LADD}_A + 91 \quad (R^2 = 0.96, \ p < 0.001) & \text{Equation 8.4} \\
CP &= 78\log\text{LADD}_T + 86 \quad (R^2 = 0.90, \ p < 0.001) & \text{Equation 8.5}
\end{align*}

The slope (113) of the linear regression line of the CPD plot for LADD\textsubscript{B} was steeper
than that (44) for LADD\textsubscript{A}. This implies that the range of the absorbed doses of
chlorpyrifos from background exposure was relatively narrow, compared to that of the
absorbed doses from occupational application. This finding was not unexpected because
background exposure to environmental chemicals in a population are usually from
common sources such as food, water, and air with a consistent pattern of exposure
(Macintosh et al., 2001; Whyatt et al., 2002; Eaton et al., 2008). On the contrary,
exposure from occupational sources usually vary significantly at an individual
applicator level, depending on factors such as the quantities of pesticides applied as well
as the pesticide handling practices (Solomon et al., 2005).

The exposure dose at the 50\textsuperscript{th} percentile (CP\textsubscript{50}) and the 95\textsuperscript{th} percentile (CP\textsubscript{95}) describes
the levels of exposure among the median exposed and the 5\% highly-exposed groups,
respectively. The dose at CP\textsubscript{50} for LADD\textsubscript{B}, LADD\textsubscript{A} and LADD\textsubscript{T} were 0.2 µg/kg/day,
0.1 µg/kg/day and 0.4 µg/kg/day, respectively. At CP₉₅, the dose was 2 µg/kg/day, 1 µg/kg/day and 3 µg/kg/day for LADD₉, LADDₐ and LADD₇, respectively.
Figure 8.5: Cumulative Probability Distribution (CPD) Plots of Chlorpyrifos Chronic Exposure Levels (LADD_B, LADD_A and LADD_T) among Applicators on Rice Farms in Ghana.
The CPD plots of ADD\textsubscript{A} and ADD\textsubscript{T} are presented in Figures 8.6 A and B, receptively. The regression lines of the linear parts of the plots were represented by the following equations:

\begin{align*}
CP &= 44\log(ADD\textsubscript{A}) + 11 \quad (R^2 = 0.97, \ p < 0.001) \quad \text{Equation 8.6} \\
CP &= 46\log(ADD\textsubscript{T}) + 9 \quad (R^2 = 0.97, \ p < 0.001) \quad \text{Equation 8.7}
\end{align*}

where, CP is the cumulative probability (%).

The linear part of the CPD plots of ADD\textsubscript{A} and ADD\textsubscript{T} in this study, were all determined to lie between 5\textsuperscript{th} and 95\textsuperscript{th} percentiles of the CPD, respectively. The slope (44 and 46, respectively) and the $R^2$ values (0.97) of the two regression lines were alike, suggesting that the distribution of ADD\textsubscript{A} and ADD\textsubscript{T} were similar. This is a result of the ADD\textsubscript{B} making a minor contribution to ADD\textsubscript{T} which is mainly due to the ADD\textsubscript{A}. The dose at CP\textsubscript{50} for both ADD\textsubscript{A} and ADD\textsubscript{T} were the same (8 \mu g/kg/day), whereas, the dose at CP\textsubscript{95} for the two exposure scenarios were different at 83 \mu g/kg/day and 74 \mu g/kg/day, respectively.
Figure 8.6: Cumulative Probability Distribution Plot of Chlorpyrifos Acute Exposure Levels (ADD$_A$ and ADD$_T$) among Applicators on Rice Farms in Ghana.
8.2.3 Risk Characterization with the Hazard Quotient (HQ) Technique Using Guideline Values

Chlorpyrifos Guideline Values Used

The HQ values were calculated using chlorpyrifos guideline values of the WHO and USEPA (Table 7.1, Section 7.2). These two agencies are generally among the foremost in the field of health risk assessment, with the WHO being concerned with global issues and USEPA with national issues. Countries without their own national guideline values rely on those set by these institutions for health risk assessment evaluations. According to the WHO, the acute and chronic guideline values of chlorpyrifos are 100 µg/kg/day and 10 µg/kg/day, respectively (WHO, 2009). However, much lower guideline values have been set by the USEPA. The acute guideline value is set at 5 µg/kg/day, while the chronic guideline value is set at 0.3 µg/kg/day (USEPA, 2000). The differences in the guideline values of the two organisations are because of the different toxicological endpoints and safety factors used to derive the values (Sections 7.2).

Hazard Quotient Values for Acute Exposure to Chlorpyrifos

The HQ values obtained for acute exposure to chlorpyrifos are presented in Table 8.3. Using the acute guideline value of the WHO, HQ$_{50}$ (0.08) and HQ$_{95}$ (0.8 and 0.7) for the acute exposure scenarios (ADD$_A$ and ADD$_T$, respectively) were all less than unity. However, according to the acute guideline value of the USEPA, both HQ$_{50}$ (1.6) and HQ$_{95}$ (16.6 and 14.7, respectively) for the two acute exposure scenarios were above unity. The HQ obtained with the acute guideline value of the WHO therefore suggests that there is less likelihood for occurrence of acute adverse health effects among both...
the median and the 5% highly-exposed groups, under ADD_A and ADD_T scenarios. In contrast, the HQ calculated with the acute guideline value of the USEPA suggest that both the median and the 5% highly-exposed groups were at high risk of acute health effects under both ADD_A and ADD_T scenarios.

Hazard Quotient Values for Chronic Exposure to Chlorpyrifos

The HQ values obtained for chronic exposure to chlorpyrifos are also presented in Table 8.3. The values for HQ_{50} (0.02, 0.01, and 0.04) and HQ_{95} (0.2, 0.2, and 0.3) calculated using the chronic guideline value of the WHO, were less than unity for all the three chronic exposure scenarios (LADD_B, LADD_A, and LADD_T, respectively). These indicate that there was low risk of chronic health effects among the median and the 5% highly-exposed groups, under all the chronic exposure scenarios.

With the chronic guideline value of the USEPA, HQ_{50} values (0.7 and 0.4) were less than unity for both LADD_B scenario (chronic exposure from background chlorpyrifos) and LADD_A scenario (chronic exposure from occupational application of chlorpyrifos), respectively. HQ_{50} was however, more than unity (HQ_{50}, 1.2) for LADD_T scenario (chronic exposure from background chlorpyrifos and occupational application of chlorpyrifos). These findings imply that when considered separately, background exposure and occupational exposure to chlorpyrifos constituted less risk of chronic health effects among the median exposed group, using the USEPA chronic guideline value. However, when considered together, the resulting exposure posed a risk of chronic health effects among the median exposed group. The HQ_{95} obtained with the USEPA chronic guideline value for all the chronic exposure scenarios (LADD_B,
LADD_A and LADD_T) were above unity. Therefore, this suggests that background exposure and occupational exposure to chlorpyrifos among the 5% highly exposure group posed high risk of chronic adverse health effects, when considered separately as well as together.

Table 8.3: Hazard Quotient Values of Chlorpyrifos Exposure Levels at CP50 and CP95 with Rice Farmers in Ghana

<table>
<thead>
<tr>
<th>Exposure Dose (µg/kg/day)</th>
<th>Exposure Dose (µg/kg/day)</th>
<th>Hazard Quotient Value</th>
<th>Hazard Quotient Value</th>
<th>Hazard Quotient Value</th>
<th>Hazard Quotient Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HQ50</td>
<td>HQ95</td>
<td>HQ50</td>
<td>HQ95</td>
</tr>
<tr>
<td>ADD_A</td>
<td>CP50</td>
<td>CP95</td>
<td></td>
<td>HQ50</td>
<td>HQ95</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>83</td>
<td></td>
<td>0.08</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>ADD_T</td>
<td>8</td>
<td>74</td>
<td>0.08</td>
<td>0.7</td>
</tr>
<tr>
<td>Chronic Scenario</td>
<td></td>
<td>HQ50</td>
<td>HQ95</td>
<td>HQ50</td>
<td>HQ95</td>
</tr>
<tr>
<td>LADD_B</td>
<td>CP50</td>
<td>CP95</td>
<td></td>
<td>HQ50</td>
<td>HQ95</td>
</tr>
<tr>
<td></td>
<td>0.2</td>
<td>2</td>
<td></td>
<td>0.02</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>LADD_A</td>
<td>0.1</td>
<td>1</td>
<td>0.01</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>LADD_T</td>
<td>0.4</td>
<td>3</td>
<td>0.04</td>
<td>0.3</td>
</tr>
</tbody>
</table>

(HQ values > 1 are coloured red)

8.2.4 Risk Characterization with the HQ Technique Using TSD Dose at CP5

The CPD plots of the chronic exposure doses and TSD_Chronic are shown in Figure 8.7, while the CPD plots of the acute exposure doses and TSD_Acute are shown in Figure 8.8. The HQ values calculated based on Figures 8.7 and 8.8 are presented in Table 8.4.

The HQ50/5 values obtained for chlorpyrifos chronic exposure from background (LADD_B), occupational application (LADD_A) as well as from the combined exposure
from background and occupational application (LADD\textsubscript{T}) were all less than unity (0.4, 0.2 and 0.8, respectively).

These suggest that, there was no or little risk of chronic adverse effects due to chlorpyrifos exposure under the above scenarios (LADD\textsubscript{B}, LADD\textsubscript{A} and LADD\textsubscript{T}) among the median exposed group of the applicators. However, the HQ\textsubscript{95/5} value obtained for above exposure scenarios were all above unity (4, 2 and 6 for LADD\textsubscript{B}, LADD\textsubscript{A} and LADD\textsubscript{T}, respectively). These imply that, there were risks of chronic adverse effects due to chlorpyrifos exposure from background, occupational application and from the combined exposure from these two sources among the 5% highly-exposed group of the applicators.

For the acute exposure scenarios, HQ\textsubscript{50/5} values for both ADD\textsubscript{A} and ADD\textsubscript{T} were the same (4) and above unity. Likewise, the values for HQ\textsubscript{95/5} (42 and 37, respectively) for two acute scenarios were above unity. This was particularly significant in the case of acute exposure. These show that there were risks of acute adverse effects among both the median exposed and the 5% highly-exposed groups due chlorpyrifos exposure from occupational application (ADD\textsubscript{A}) and from the combined exposure from background and occupational application (ADD\textsubscript{T}).
Figure 8.7: Cumulative Probability Distribution (CPD) Plots of ADD_B, ADD_A and ADD_T Levels of Chlorpyrifos among Applicators on Rice Farms in Ghana, as well as Chlorpyrifos TSD_{CHRONIC} from Human Epidemiological Studies.
Figure 8.8: Cumulative Probability Distribution (CPD) Plots of ADD\textsubscript{A} and ADD\textsubscript{T} Levels of Chlorpyrifos among Applicators on Rice Farms in Ghana, as well as Chlorpyrifos TSD\textsubscript{ACUTE} from Human Epidemiological Studies.
Table 8.4: HQ\textsubscript{50/5} and HQ\textsubscript{95/5} Values for Chlorpyrifos Exposure Levels among Applicators on Rice Farms in Ghana.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>CP\textsubscript{50} of Exposure (µg/kg/day)</th>
<th>CP\textsubscript{95} of Exposure (µg/kg/day)</th>
<th>CP\textsubscript{5} of TSD (µg/kg/day)</th>
<th>Hazard Quotient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Scenario</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LADD\textsubscript{B}</td>
<td>0.2</td>
<td>2</td>
<td>0.5</td>
<td>4</td>
</tr>
<tr>
<td>LADD\textsubscript{A}</td>
<td>0.1</td>
<td>1</td>
<td>0.5</td>
<td>2</td>
</tr>
<tr>
<td>LADD\textsubscript{T}</td>
<td>0.4</td>
<td>3</td>
<td>0.5</td>
<td>6</td>
</tr>
<tr>
<td>Acute Scenario</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADD\textsubscript{A}</td>
<td>8</td>
<td>83</td>
<td>2</td>
<td>4 42</td>
</tr>
<tr>
<td>ADD\textsubscript{T}</td>
<td>8</td>
<td>74</td>
<td>2</td>
<td>4 37</td>
</tr>
</tbody>
</table>

(HQ values > 1 are coloured red)

8.2.5 Risk Characterization with Probabilistic Techniques

In the previous Sections in this Chapter the health risk from chlorpyrifos exposure has been characterized using the HQ technique which focused on the most sensitive or most exposed applicator groups. In this Section, the risk will be characterized with probabilistic techniques using all exposure levels and expected sensitivities of the whole population of applicators. Two techniques were used to do this – Overall Risk Probability and the Monte Carlo Simulation techniques.

Risk Output from the Overall Risk Probability (ORP) Technique

The details of the Overall Risk Probability (ORP) technique and its application in this study are explained in Section 4.9.3. With this technique, the distribution of both exposure and Toxicant Sensitivity Distribution (TSD) are plotted on the same graph.
Exposure Exceedance values at any dose level are then calculated and the corresponding percentages of the population exhibiting adverse effects (Affected Population) at these exposure exceedance values are identified. The Exposure Exceedance values are subsequently plotted against the percentage of the Affected Population, to produce an ORP curve. The area under the ORP curve is then calculated as the ORP value, which represents the proportion of the population who are at risk of adverse effects (Cao et al., 2011).

In this study, exposure exceedance values and the corresponding percentages of population expected to exhibit adverse effects at the various exposure exceedance values were obtained from Figure 8.7 and 8.8 for chronic exposures and acute exposures, respectively. The obtained values were used to plot the ORP curves and are shown in Figure 8.10. With chronic exposures, ORP values of 3%, 4% and 8% were obtained for LADD_B (background exposure), LADD_A (chronic exposure from occupational application) and LADD_T (total chronic exposure from background and occupational exposure), respectively. Regarding acute exposures, the ORP values obtained for ADD_A (acute exposure from occupational application) and ADD_T (total acute exposure from both background and occupational application) were 31% and 32%, respectively. The obtained values represent the proportion of the applicators that were likely to suffer adverse health effects under the chronic and acute exposure scenarios evaluated.

Using the data utilized for the TSD plot in Section 7.3 (Table 7.2), possible adverse effects can be suggested from those observed in previous investigations. Acute adverse
effects likely to be suffered by the applicators of this study may include depression of cholinesterase activity, sub-clinical neuropathy and memory problems due to acute exposures (Steenland et al., 2000; Albers et al., 2007; Farahat et al., 2011); whereas chronic adverse effects may include fetal neurodevelopment defects, altered thyroid functions and reductions in estradiol levels (Berkowitz et al., 2004; Meeker et al., 2006; Meeker et al., 2008).

The proportion of the applicators likely to suffer adverse effects due to chlorpyrifos exposure from chronic background exposure (3%), chronic exposure from occupational application (4%), and acute exposure from occupational application (31%) are comparable to those reported by Phung et al. (2013) among Vietnamese rice farmers under similar exposure scenarios (1%, 2% and 29%, respectively).
Risk Output from the Monte-Carlo Simulation Technique

The procedure involved with the use of Monte-Carlo Simulation (MCS) technique is explained in detail in Section 4.9.4. Using the means and standard deviations of the exposure and TSD data, Hazard Quotient (HQ\textsubscript{MCS}) values were simulated 10,000 as the ratio of exposure dose to toxicant sensitivity dose for a range of dose levels. The simulations were performed using Oracle Crystal Ball\textsuperscript{®} Monte Carlo software, based on log-normal distributions. The probability of HQ\textsubscript{MCS} values exceeding unity constituted the proportion of the population at risk of adverse effects.
The descriptive statistics of the \( HQ_{MCS} \) values obtained from the simulation are provided in Table 8.5. With the chronic exposure scenarios, the mean \( HQ_{MCS} (\pm S.E.M) \) values obtained for chlorpyrifos exposure from background (LADD\(_B\)), occupational application (LADD\(_A\)) and from the combined exposure from background and occupational application (LADD\(_T\)) were 0.12 (± 0.00), 0.15 (± 0.00) and 0.28 (± 0.01), respectively. For the acute exposure scenarios, the \( HQ_{MCS} (\pm S.E.M) \) values obtained were 2.49 (± 0.11) and 2.19 (± 0.0) for chlorpyrifos exposure from occupational application (ADD\(_A\)) and from the combined exposure from background and occupational application (ADD\(_T\)), respectively.

Table 8.5: Descriptive Statistics of Monte Carlo Simulation Hazard Quotient (HQ\(_{MC}\)) Values for Chlorpyrifos Exposures among Applicators on Rice Farms in Ghana.

<table>
<thead>
<tr>
<th>Exposure Scenario</th>
<th>Descriptive Statistics for HQ(_{MCS}) Values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>LADD(_B)</td>
<td>0.12</td>
</tr>
<tr>
<td>LADD(_A)</td>
<td>0.15</td>
</tr>
<tr>
<td>LADD(_T)</td>
<td>0.28</td>
</tr>
<tr>
<td>ADD(_A)</td>
<td>2.49</td>
</tr>
<tr>
<td>ADD(_T)</td>
<td>2.19</td>
</tr>
</tbody>
</table>

Graphical representations of the probability distributions of the HQ\(_{MCS}\) values from Table 8.5 are shown in Figures 8.10 and 8.11. HQ\(_{MCS}\) values less or equal to unity constitute no adverse health risk, while HQ\(_{MCS}\) values more than unity constitute adverse health risk. The probability (or certainty) of the HQ\(_{MCS}\) values being less or equal to unity (i.e. from infinity to 1) for LADD\(_B\), LADD\(_A\), LADD\(_T\), ADD\(_A\) and ADD\(_T\)
scenarios were approximately 99%, 98%, 95%, 67% and 66%, respectively (Figures 8.10 and 8.11). Therefore, the probability of HQMCS values exceeding 1 (i.e. occurrence of adverse health effect) among the applicators for LADD<sub>B</sub>, LADD<sub>A</sub>, LADD<sub>T</sub>, ADD<sub>A</sub> and ADD<sub>T</sub> scenarios were 1%, 2%, 5%, 33% and 34% for LADD<sub>B</sub>, LADD<sub>A</sub>, LADD<sub>T</sub>, ADD<sub>A</sub> and ADD<sub>T</sub> scenarios, respectively.
Figure 8.10: Probability Distribution of $HQ_{MCS}$ Values for Chronic Exposure (LADD$_B$, LADD$_A$ and LADD$_T$) Levels of Chlorpyrifos. The probability of $HQ_{MCS}$ exceeding unity was 1%, 2% and 5% for LADD$_B$, LADD$_A$ and LADD$_T$, respectively. The red arrows show the ranges where $HQ_{MCS}$ exceeded unity.
Figure 8.11: Probability Distribution of HQ_{MCS} Values for Acute Exposure (ADD_{A} and ADD_{T}) Levels of Chlorpyrifos. The probabilities of HQ_{MCS} exceeding unity were 33% and 34% for ADD_{A} and ADD_{T}, respectively. The red arrows show the ranges where HQ_{MCS} exceeded unity.
Comparison of Risk Outputs from the ORP and MCS Techniques

The HQ techniques are targeted at identifying the risk of adverse effects among specific exposure groups using a fixed guideline value set at a minimum. The exposure groups are the median-exposed group (50th percentile) and the 5% highly-exposed group (95th percentile). Consequently, risk outputs from the HQ techniques are not comparable to those from the ORP and MCS techniques, since the ORP and MCS outputs evaluate overall health risk for the whole population with different sensitivities and exposures. The overall risk output from the ORP and MCS techniques for the exposure scenarios evaluated are shown in Table 8.6.

The risk outputs of the ORP and the MCS techniques in this study were generally similar. Comparable trends have been reported by Phung et al. (2013). In the study by Phung et al. (2013), the overall risk value obtained with the ORP and MCS techniques for post-application exposure to chlorpyrifos was 31% and 33%, respectively. The similarity in the risk output from the ORP and the MSC techniques results from both techniques utilizing all dose ranges of exposure and toxicant sensitivity.
Table 8.6: Risk Outputs as Proportion of the Applicator Population (%), Using the ORP and MCS Techniques.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Proportion of Overall Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ORP</td>
</tr>
<tr>
<td><strong>Chronic Scenario</strong></td>
<td></td>
</tr>
<tr>
<td>LADD_B</td>
<td>3</td>
</tr>
<tr>
<td>LADD_A</td>
<td>4</td>
</tr>
<tr>
<td>LADD_T</td>
<td>8</td>
</tr>
<tr>
<td><strong>Acute Scenario</strong></td>
<td></td>
</tr>
<tr>
<td>ADD_A</td>
<td>31</td>
</tr>
<tr>
<td>ADD_T</td>
<td>32</td>
</tr>
</tbody>
</table>

Comparison of Risk Outputs from the ORP and MCS Techniques Against Applicators’ Self-Reported Pesticide Symptoms

It should be noted that the health risk estimates from the ORP and MCS techniques were attributable to chlorpyrifos exposure only. However, other common types of pesticides used by the applicators included 2,4-D, bispyribac-sodium, glyphosate and lambda-cyhalothrin (Section 5.3). With the unsafe pesticide handling practices reported in Sections 5.4, 6.1.2 and 6.2.2, the applicators were likely to be exposed to these other pesticides in addition to chlorpyrifos. Owing to additive and synergistic health effects of pesticides (Cedergreen, 2014; Ilboudo et al., 2014; Rizzati et al., 2016), the proportion of the applicators that were likely to suffer health effects would be expected to be more than the 31% and 33% suggested by the ORP and MCS health risk estimates, respectively. In fact, it is reported in Section 5.5 that following pesticide application, all applicators of the study had experienced symptoms compatible with acute pesticide poisoning, according to the descriptions of the Intergovernmental Forum on Chemical Safety (IFCS) of the WHO (Thundiyil, 2008). The commonest of the symptoms were
excessive tiredness, blurred vision, skin rashes, headache, dizziness and sleeping difficulty.

8.2.6 Summary

Various techniques have been employed in this Section to characterize health risks due to chlorpyrifos exposure under different scenarios among the applicators in the study group. These techniques included HQ, ORP and MCS techniques. The HQ techniques were aimed at identifying risk of health effects among the median-exposed (50th percentile) and the 5% highly-exposed (95th percentile) groups. On the other hand, the ORP and MCS techniques aimed at quantifying the overall proportion of the study population that were at risk of health effects. The risk outputs of the techniques are summarized in Table 8.7.

Table 8.7: Summary of Outputs from All the Risk Characterization Techniques Used.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>HQ with WHO’s Guideline Values</th>
<th>HQ with USEPA’s Guideline Values</th>
<th>HQ with CP5</th>
<th>Overall Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HQ50</td>
<td>HQ95</td>
<td>HQ50</td>
<td>HQ95</td>
</tr>
<tr>
<td>Chronic Scenario</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LADD_B</td>
<td>0.02</td>
<td>0.2</td>
<td>0.7</td>
<td>6.5</td>
</tr>
<tr>
<td>LADD_A</td>
<td>0.01</td>
<td>0.1</td>
<td>0.4</td>
<td>4.0</td>
</tr>
<tr>
<td>LADD_T</td>
<td>0.04</td>
<td>0.3</td>
<td>1.2</td>
<td>10.4</td>
</tr>
<tr>
<td>Acute Scenario</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADD_A</td>
<td>0.08</td>
<td>0.8</td>
<td>1.6</td>
<td>16.6</td>
</tr>
<tr>
<td>ADD_T</td>
<td>0.08</td>
<td>0.7</td>
<td>1.6</td>
<td>14.7</td>
</tr>
</tbody>
</table>

(HQ values > 1 and the overall risk values are coloured red)
With the exception of the HQ technique based on the WHO’s guideline values, the remainder of the techniques suggested significant health risk among the applicators. The HQ technique based on the USEPA’s guideline value suggested risk of chronic health effects among the median-exposed group from the combined chlorpyrifos exposure from background and occupational application ($LADD_T$), as the HQ value exceeded unity ($HQ_{50} 1.2$). Also, the HQ technique based on both the USEPA’s guideline value and CP₅ suggested risk of chronic health effects among the 5% highly-exposed group, due to exposure from background ($LADD_B$) ($HQ_{95} 6.5$ and $HQ_{95/5} 4$), occupational application ($LADD_A$) ($HQ_{95} 4$ and $HQ_{95/5} 2$), as well as from the combined exposure from background and occupational application ($LADD_T$) ($HQ_{95} 10.4$ and $HQ_{95/5} 6$).

With acute health effects, the HQ technique based on both the USEPA’s guideline value and CP₅ suggested risks among the median-exposed group ($HQ_{50} 1.6$ and $HQ_{95/5} 4$) and the 5% highly-exposed group ($HQ_{95} 16.6$ and $HQ_{95/5} 42$), due to exposure from occupational application ($ADD_A$). Also, risks of acute health effects are suggested due to the combined exposure from background and occupational application ($ADD_T$) among the median-exposed group ($HQ_{95} 14.7$ and $HQ_{95/5} 37$).

Overall, the ORP and MCS techniques quantified the proportions of the applicators that were likely to exhibit chronic health effects due to chlorpyrifos exposure from background, occupational application and the combined exposure from background and occupational application, to range from 1 to 3%, 2 to 4% and 5 to 8%, respectively. With acute health effects, the ORP and MCS estimated the proportions of the
applicators that were likely to suffer due to exposure from occupational application and from the combined exposure from background as well as occupational application, to range between 31 to 33% and 32 to 34%, respectively.
CHAPTER 9
GENERAL CONCLUSIONS AND RECOMMENDATIONS

9.1 Introduction

The conceptual framework of this research, based on the four-step health risk assessment framework of the United States’ National Research Council (USEPA, 2000; NRC, 2009), is shown in Figure 4.1 of Section 4.2 and repeated in this chapter as Figure 9.1. The figure illustrates how the chapters and sections of the research fit into the conceptual framework. The main objectives of the overall research were to:

1. Identify hazardous pesticides and practices associated with the use of pesticides among applicators;
2. Assess the levels of chlorpyrifos exposure among applicators;
3. Evaluate the patterns of dermal exposure to chlorpyrifos among applicators;
4. Review the dose-response relationship of chlorpyrifos exposure and adverse effects;
5. Characterize the risks of adverse health effects due to chlorpyrifos exposure among applicators;

Hazard identification study was carried out to identify the principal pesticide used and hazardous pesticide handling practices (Chapter 5). Based on these findings, chlorpyrifos, a moderately toxic insecticide, was identified as the most commonly used pesticide by applicators and likely to present a major hazard. Thus, exposure assessments were carried out to evaluate the levels of chlorpyrifos exposure among the
applicators (Chapter 6). Dose-response evaluations of data from the scientific literature were undertaken to quantitatively describe the toxicity of chlorpyrifos, through collation of Guideline Values (GVs) obtained with the No Observable Adverse Effect Level (NOAEL) and Toxicant Sensitivity Distributions (TSDs) techniques (Chapter 7). Using the results from these exposure and dose-response evaluations, risk characterizations were performed to quantify the risks of adverse health effects among the applicators (Chapter 8).

The objective of Chapter 9, highlighted with green colour in Figure 9.1, is to summarize and integrate the conclusions of the previous chapters and provide strategies that can assist management of pesticide exposure among applicators in Ghana and other developing countries.
Figure 9.1: The Section on Conclusions and Recommendations (highlighted with green colour in the overall research framework) (see Figure 4.1 in Section 4.2).
9.2 General Conclusions

Hazard Identification

The first step in this research was to identify pesticide hazards to rice farmers in Ghana. The hazard identification study in Chapter 5 showed that use of chemical pesticides is the main pest control strategy among the farmers, with chlorpyrifos being the most widely used pesticide with 83% usage prevalence. This study showed that pesticides were applied under unsafe conditions, which included inadequate use of personal protective equipment (78%); frequent spillages and leakages during use (90%); low level of training on pesticides safety (40%); and low educational attainment (61%). The study also showed that all applicators had experienced symptoms that were compatible with pesticide poisoning as described by the WHO (Thundiyil, 2008).

Exposure Assessment

Whole-Body Dermal Exposure Assessment

The dermal exposure study (Section 6.1, Chapter 6) showed that the levels of Total Dermal Exposure (TDE) and the corresponding percentage Unit Exposure (UE) values among the applicators were higher than those for similar exposure scenarios described in the USEPA’s Pesticide Handlers Exposure Database (PHED), a commonly used exposure model. Usage of such exposure models under settings applicable in Ghana, as well as other developing countries, may therefore under-estimate the levels of pesticide exposure. The present study also indicated that the hands (39% of TDE) and the lower anatomical (82% of TDE) regions of the applicators were the most exposed. The levels
of dermal exposure were influenced by the quantity of insecticide applied and the height of the crops sprayed (p < 0.05).

**Urinary TCP Assessment of Overall Chlorpyrifos Exposure**

After reaching a maximum concentration, the decline of post-application chlorpyrifos with time, was found to follow first-order kinetics (Section 6.2 of Chapter 6). The elimination half-life \( t_{1/2} \) of chlorpyrifos was calculated to be 50 hours, which was higher than those reported in previous studies at 27 to 43 hours. The half-life obtained indicates that the levels of chlorpyrifos found with applicators would be expected to return to background levels about 10 days after exposure. Therefore, the standard sampling duration of 5 days for biological monitoring of chlorpyrifos may lead to under-estimation of the exposure levels.

Following a spray event, the median absorbed daily dose of chlorpyrifos \( (ADD_A) \) (6 µg/kg/day) increased about 30-fold, compared to the baseline level \( (LADD_B) \) (0.2 µg/kg/day). The levels of chlorpyrifos absorbed dose from occupational application were influenced by the quantity of chlorpyrifos formulation applied, spraying duration, and the number of spray tanks applied (p < 0.05).

The Absorbed Daily Dose \( (ADD) \) of chlorpyrifos estimated from the whole-body dermal dosimetry and urinary TCP evaluations produced similar exposure estimates, based on the mean chlorpyrifos dose (16 and 15 µg/kg/day, respectively) of applicators who participated in both evaluations. In accord with other investigations, this
demonstrates that the dermal route is the major exposure route for applicators. However, the dose estimates from the dermal dosimetry were generally higher than those for the urinary TCP below the 75th percentile but lower than the estimates from the urinary TCP above the 75th percentile.

**Dose-Response Assessment and Toxicant Sensitivity Distributions (TSD) Assessment**

Various guideline values derived by regulatory agencies (WHO, USEPA, and APVMA) for evaluating health risks of chlorpyrifos exposure in human populations were identified from the scientific literature. The chronic guideline values derived with conventional No Observable Adverse Effect Level (NOAEL) method ranged from 0.3 to 10 µg/kg/day. With acute guidelines, the values established varied from 5 to 100 µg/kg/day. The differences in the guideline values depended on the toxicological endpoints and safety factors applied. With the use of Toxicant Sensitivity Distributions (TSDs) method based on human epidemiological data of chlorpyrifos, chronic and acute guideline values of 0.5 and 2 µg/kg/day were derived, respectively. Unlike the guideline values derived based on the NOAEL method, the ones derived with the TSD method are directly applicable to humans without the need for safety factors.

**Health Risk Characterization**

With the exception of the HQ values (HQ < 1) derived with the WHO’s guideline values, the HQ values (HQ > 1) obtained with the guideline values of the USEPA, APVMA, as well as the TSD threshold dose at CP₅ suggested excessive exposure
among the applicators, with consequent acute and chronic health risks. This was particularly true among the 5% highly exposed group (HQ 4 to 42). The proportions of the applicators that were likely to suffer chronic health effects due to chlorpyrifos exposure from background, occupational application and combined exposure, from background and occupational application, were estimated by the ORP and MSC techniques to range from 1 to 3%, 2 to 4% and 5 to 8%, respectively. Such chronic health effects may include altered thyroid functions and reductions in estradiol levels as indicated by the TSD. With acute health effects, the ORP and MCS techniques estimated the proportions of the applicators that were likely to suffer due to exposure from occupational application and from combined exposure including background, to range between 31 to 33% and 32 to 34%, respectively. The acute health effects likely to be suffered by the applicators can include depression of cholinesterase activity, sub-clinical neuropathy and memory problems, particularly with occupational exposure as indicated in the TSD.

9.3 Recommendations for Improving Pesticide Safety

The applicators were found to be exposed to excessive levels of chlorpyrifos and therefore some interventions are needed to minimize exposure. Improvement in pesticide safety would require implementation of various strategies by all stakeholders concerned. The following recommendations are made for consideration by government officials, applicators and the research community, based on the findings of this study as well as other relevant investigations.
9.3.1 Recommendations to Government of Ghana

Improving Adoption of Integrated Pest Management (IPM)

Integrated Pest Management (IPM) has been widely accepted at an official level as the best approach for managing agricultural pests (World Bank, 2005). Although IPM has been adopted as the most appropriate pest management strategy for Ghana, the approach is not practiced by the farmers, as use of pesticides remained the dominant pests control strategy. The Ministry of Food and Agriculture (MoFA) and other relevant stakeholders should therefore facilitate the provision of training and technical services to farmers to enhance IPM adoption.

Promoting Use of Less Toxic Pesticides

Although majority of the pesticides used by the farmers in this study belonged to WHO Toxicity Classes II (moderately hazardous), III (slightly hazardous) and U (unlikely to present acute hazard in normal use), there were evidence of usage of WHO Toxicity Classes Ib (highly hazardous) and obsolete hazardous pesticides. Use of less toxic pesticides, such as biopesticides (Boeke et al., 2004; Chaudhary et al., 2017), should be promoted. Also, strengthening border control mechanisms would help prevent unapproved pesticides from being imported into the country.

Training Farmers and Agricultural Extension Officers (AEOs) on Pesticide Safety

The educational level of majority (61%) of the farmers was low (up to Junior High School). Therefore, these farmers may not be able to read and understand pesticide
labels. Providing the farmers with adequate training on pesticides safety may help them appreciate the health risk associated with pesticides as well as the strategies for minimising exposure. Also, adequate education on pesticide safety should be given to Agricultural Extension Officers (AEOs) to ensure that farmers are in turn trained adequately and properly.

**Regular Monitoring of Pesticide Exposure**

This study is the first to provide information on the levels of pesticide exposure among applicators in Ghana. It is proposed that such exposure monitoring programs should be carried out on a regular basis. This would enable policy makers and other stakeholders in the country to better understand the magnitude of pesticide exposure and associated health problems. Moreover, such programs would help to identify appropriate interventions to improve pesticide safety in the country. The monitoring programs should be mandatory for applicators in the large-scale formal agricultural sector, with employers paying for the cost. Applicators in the small-scale informal sector may not be able to pay for the cost of such monitoring programs and therefore may require some assistance or a different arrangement.

The cost and technical requirements of biological exposure monitoring programs may not be practical in Ghana. However, less-expensive exposure monitoring programs such as the whole-body dermal dosimetry can be used. The laboratory analysis of the dermal dosimetry samples was carried out at the Pesticides Residues laboratory of Ghana Standards Authority (GSA). Therefore, the laboratory staff of GSA are now equipped with the techniques for the analysis, which can be applied in exposure monitoring
programs in Ghana. This study has demonstrated that the whole-body dermal dosimetry provides valid information regarding typical levels of exposure among applicators. The hands and lower anatomical regions were identified as the most important parts of the body that were highly exposed. Thus, as a result of the present study, a simplified program may be designed which would involve monitoring of contamination of these anatomical regions as representative of whole body exposure.

9.3.2 Recommendations to Pesticide Applicators

Use of Adequate PPE

Use of PPE is preferably the last option for protection against exposure. However, it is the most practical option for most small-scale farmers in many developing countries. PPE usage rate among the farmers of this study was very low (22%). The only type of PPE used by the applicators was safety glasses, which is inadequate to offer appreciable level of protection, apart from protecting the eyes. It is therefore recommended that applicators should frequently use adequate PPE when handling and applying pesticides, to reduce exposure. Wearing hand gloves may significantly reduce exposure, since the hands received the highest level of exposure among the applicators.

Avoiding Excessive Pesticide Use and Reducing Spray Duration

This study has shown that the levels of pesticide exposure can be significantly influenced by the quantity of the pesticide formulation applied. Ensuring that recommended pesticides application rates for crops are adhered to, can be a way to reduce excessive use. Also, spray equipment should be regularly maintained and
calibrated to avoid excessive flow rate and leakages. To reduce spray duration, applicators can form teams for mutual assistance during spraying, particularly for those that work on large farms.

**Reducing the Number of Spray Tanks**

The study identified that the higher the number of spray tanks filled by the applicators, the higher the levels of exposure. This suggested that loading and mixing may be associated with increased exposure. Applicators can reduce the number of spray tanks or loading and mixing activities by using 20-litre spray equipment instead of the 15 or 16-litre equipment used.

**Good Hygiene Practices**

Incidences of spillage and leakages were common among the applicators. Exposures through such incidences may be significantly reduced through good hygiene practices, including showering and changing farm clothing immediately after accidental contamination and spraying (Gomes *et al.*, 1999; Koureas *et al.*, 2014).

**9.3.3 Recommendations to Researchers**

It is recommended that the scientific community in Ghana with expertise in exposure assessment should partner with Government and provide required technical support for implementation of pesticide exposure monitoring programs in the country.
Currently, no epidemiological studies have been conducted to evaluate the adverse health effects of pesticides among applicators in Ghana. With the high levels of exposure established in the present study, further studies on pesticide related adverse effects among applicators in Ghana would help to reveal the full extent of the public health implications of pesticides in the country. Also, clinical studies aimed at measuring the levels of cholinesterase inhibition among the applicators would be useful.
APPENDICES
Appendix 1: Participant Information Sheet

Centre for Environment and Population Health (CEPH)

Participant Information Sheet

Project Title
Health Risk Assessment and Management of Chlorpyrifos Exposure among Rice Farmers in Ghana.

Primary Investigator:
Albert Atabila, MPH, MOSH (PhD Student)
Centre for Environment and Population Health
School of Environment, Griffith University, Queensland
Email: albert.atabila@griffithuni.edu.au

Objective
The objective of this study is to evaluate the health risk due to organophosphate insecticides (OP) among farmers in Ghana. The result of this evaluation would provide not only knowledge of health risk due to pesticide but also useful information for the most effective management of occupational health and safety among farmers in Ghana.

Background
In Ghana, pesticides are heavily used by farmers, with chlorpyrifos being among the most commonly used. There is however a general lack of studies that assess pesticide exposure and the associated health risk among farmers. The study seeks to evaluate the risk of organophosphate insecticides among farmers who are directly involved in spraying pesticides on their crops in Ghana.

Method
Exposure assessment will be done through urine analysis of pesticide metabolite. Six 24-hour urine samples will be obtained from each farmer (collection of urine in a container during normal urination) who directly sprays pesticides on their crops. Alternatively, the exposure assessment will be done by measuring dermal as well as inhalation exposure among the farmers. Dermal exposure assessment will be done using coverall, cotton hand gloves, and socks as the sampling media. Each farmer will wear these items during pesticide spraying activities. These sampling media will be removed...
at the end of the spraying activities and the pesticide residues collected on them analysed to estimate dermal exposure dose. In addition, inhalation exposure will be assessed by using personal air samplers placed within the breathing zone of the farmers during pesticide spraying activities. The air samples will then be analysed to estimate inhalation exposure dose.

In addition, information on pesticide handling practices will be obtained from interviews and field observation. Also, to identify the needs for improving pesticide safety, a qualitative needs assessment through focus group discussion and in-depth interview will be done among key informants.

**Inclusion and Exclusion Criteria**

Subjects chosen for the study will be adult farmers who apply pesticides and are in good general health.

Subjects will be excluded from the study if they have certain medical conditions and cannot work as a pesticide applicator.

**Risks**

The participants may feel a little uncomfortable when they wear coverall (overall) during pesticide spraying in a sunny day. Arrangement would be made with the participants so that their spraying activities are done in the mornings or late afternoons to minimise the impact of heat.

For researchers, there may be possibility of getting into direct contact with urine samples when not handled properly. The researcher will strictly ensure that correct sample handling procedures (such as use of hand gloves, and washing of hands with soap etc.) are followed to minimise such an occurrence.

**Benefits and Cost**

By participating in this study, each farmer will be provided with the results of the pesticide exposure level and health advice provided by a competent health staff, if necessary. Also this study will help fill knowledge gap on the health risks of pesticides use in Ghana. Cost to participants related to the project (eg transportation to submit samples) will be reimbursed.

**Confidentiality**

The study results will be kept as confidential as is possible by law. All data will be kept in the possession of the investigators. If the results of the study are published in a scientific journal, your identity will not be revealed. Subjects will not be referred to by name during research reports or study discussions. Urine samples collected would be labelled using codes in order not to reveal the identity of participants. All records will be stored in a locked filing cabinet with restricted access for a minimum of five years in a private office. All computer records are restricted by password. All left over samples shall be discarded at the end of the study.
**Sample Storage**

The urine samples may be stored and analysed at the laboratory of Queensland Health Forensic and Scientific Services. Only authorised laboratory staff and members of the research team may have access to the samples. The samples will be used strictly for the purpose of this research. Leftover urine samples will be discarded at the end of the study following standard bio-specimen disposal procedures.

**Contacting the investigators**

The research team is happy to answer any question from subjects at this time. If anyone has any queries later, please do not hesitate to contact Mr. Albert Atabila on 0540451339.

**Feedback**

The researcher will collaborate with occupational physicians of Ghana’s Ministry of Health to communicate the results back to the participants. Participants observed to have very high levels of pesticide exposure may be provided with free professional consultation and essential therapies for detoxification if necessary. Also, the study report and recommendations to improve pesticide safety will be communicated to the participants.

**Voluntary Participation**

Whether you decide to participate in the study or not, your decision will not prejudice you in any way. If you do decide to participate, you are free to withdraw your consent and discontinue your involvement at any time.

**Data Collection Duration**

Data collection for the study is planned to last for about 6 months.

**Privacy Statement**

The conduct of this research involves the collection, access and/or use of your identified personal information. As outlined elsewhere in this information sheet, your identified personal information may appear in publications/reports arising from this research that may be available to overseas recipients. This is occurring with your consent. Any additional personal information collected is confidential and will not be disclosed to third parties without your consent, except to meet government, legal or other regulatory authority requirements. A de-identified copy of this data may be used for other research purposes. However, your anonymity will at all times be safeguarded, except where you have consented otherwise. For further information consult the University’s Privacy Plan at http://www.griffith.edu.au/about-griffith/plans-publications/griffith-university-privacy-plan or telephone +61 7 3735 4375
Appendix 2: Informed Consent Form

Centre for Environment and Population Health (CEPH)

Informed Consent Form

Participant ID:

- Interview (Farmers)
- Urine Sampling (Farmers)
- Skin Exposure Measurement (Farmers)
- Focus Group Discussion (Farmers)
- In-depth Interview (Relevant Government Officials)

Research Title
Health Risk Assessment and Management of Chlorpyrifos Exposure among Rice Farmers in Ghana.

Contacts:

1. Primary Investigator-
   
   Albert Atabila, MPH, MOSH (PhD Student)
   
   Centre for Environment and Population Health
   School of Environment, Griffith University, Queensland
   Email: albert.atabila@griffithuni.edu.au
   Mobile: 0540451339

2. GHS-ERC Administrator-
   
   Hannah Frimpong
   Mobile: 0507041223

Participant Statement

I have read the Participant Information Sheet and the Consent Form. I agree to participate in the study entitled “Health Risk Assessment of Organophosphate Insecticides among Tomato Farmers in Ghana” and give my consent freely. I understand that the study will be carried out as described in the participant information sheet, a copy of which I have retained. I realise that whether or not I decide to participate is my decision. I also realise that I can withdraw from the study at any time.
and that I do not have to give any reasons for withdrawing. I have had all questions answered to my satisfaction.

Participant’s Name/Code:

Participant’s Signature/Thumb-print:

Date:

Witness’s Name (if applicable):

Witness’s Signature:

Date:

**Investigator Statement**

I certify that the participant has been given ample time to read/listen and learn about the study. All questions and clarifications raised by the participant have been addressed.

Investigator’s Name:

Investigator’s Signature:

Date:
Appendix 3: Farmer Survey Questionnaire

Introduction:

The purpose of this questionnaire is to gather information for a study titled “Health Risk Assessment and Management of Chlorpyrifos Exposure among Rice Farmers in Ghana”

All information collected shall be treated with high confidentiality and strictly for the purpose of this study. Your sincere responses shall be very much appreciated.

ID number: ___________________ Name of recorder: ___________________

Farmer’s mobile number: _______________ Farmer’s name: _______________

Today’s date: ______/_____/_______ Farmer’s Community/Locality: _______________

_________ Day _______ Month _______ Year
<table>
<thead>
<tr>
<th>SECTION A: SOCIO-DEMOGRAPHIC CHARACTERISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Gender</td>
</tr>
<tr>
<td>- Male</td>
</tr>
<tr>
<td>- Female</td>
</tr>
<tr>
<td>2. How old are you? _______________</td>
</tr>
<tr>
<td>3. What is your highest level of education</td>
</tr>
<tr>
<td>completed?</td>
</tr>
<tr>
<td>- None</td>
</tr>
<tr>
<td>- Primary School</td>
</tr>
<tr>
<td>- Junior High School</td>
</tr>
<tr>
<td>- Senior High School/Vocational School</td>
</tr>
<tr>
<td>- Tertiary</td>
</tr>
<tr>
<td>- Other <em>(please specify)</em>________</td>
</tr>
<tr>
<td>4. How much income do you earn from</td>
</tr>
<tr>
<td>your farm in a year?</td>
</tr>
<tr>
<td>GHC_______________</td>
</tr>
<tr>
<td>5. How many children (under 15 years) are</td>
</tr>
<tr>
<td>in your household? _________________</td>
</tr>
<tr>
<td>6. If there are, please state their ages</td>
</tr>
<tr>
<td>Child 1__________years</td>
</tr>
<tr>
<td>Child 2__________years</td>
</tr>
<tr>
<td>Child 3__________years</td>
</tr>
<tr>
<td>Child 4__________years</td>
</tr>
<tr>
<td>Child 5__________years</td>
</tr>
</tbody>
</table>
7. In the past 6 months, have you received any medical attention from a doctor, nurse or pharmacist?
   - [ ] Yes
   - [ ] No

8. If yes, what is/are the medical condition?
   ______________________________________________________________

9. What symptoms do you experience during or after spraying pesticides?
   - Vomiting or Nausea: [ ] Most times [ ] Sometimes [ ] Never
   - Headache: [ ] Most times [ ] Sometimes [ ] Never
   - Blurred vision: [ ] Most times [ ] Sometimes [ ] Never
   - Trembling hands: [ ] Most times [ ] Sometimes [ ] Never
   - Dizziness: [ ] Most times [ ] Sometimes [ ] Never
   - Breathing difficulty: [ ] Most times [ ] Sometimes [ ] Never
   - Tiredness: [ ] Most times [ ] Sometimes [ ] Never
   - Skin rashes/irritation: [ ] Most times [ ] Sometimes [ ] Never
   - Difficulty in sleeping: [ ] Most times [ ] Sometimes [ ] Never
   - Stomach pain: [ ] Most times [ ] Sometimes [ ] Never

   Other symptoms (reported by farmer):
   a. ____________: [ ] Most times [ ] Sometimes
   b. ____________: [ ] Most times [ ] Sometimes
   c. ____________: [ ] Most times [ ] Sometimes
   d. ____________: [ ] Most times [ ] Sometimes

10. How long does it take for the symptoms to appear after spraying?
   __________________________________________________________

11. Did you seek medical attention or buy medicine for the symptoms you experienced?
   - [ ] Yes
   - [ ] No

12. Did any of the symptoms you experienced prevent you from going to work the subsequent day?
   - [ ] Yes
   - [ ] No
13. What is the main crop that you grow?

14. What are the main types of pest that attack your crop? (Tick all that applies)
   - Insects  e.g.
   - Weeds  e.g.
   - Fungi
   - Others e.g

15. Do you use pesticides on your farm to control pests?
   - Yes
   - No

16. What proportion of your crop will you lose if you do not apply pesticides?

17. What are the main types of pesticides that you use?
   - Insecticides:
   - Weedicides:
   - Fungicides:
   - Others:

18. How many years have you been applying pesticides to your crops?

19. What spraying equipment do you use?
   - Knapsack sprayer
   - Motor-pressurized backpack
   - Others(specify)

20. Are you involved in the following activities regarding pesticide use?(Tick all that applies)
   - Mixing
   - Loading
   - Spraying
   - Washing of spraying equipment
   - Others(specify)

21. How many seasons do you farm in a year?

22. How many times do you apply pesticides to your crops per season?
   - Insecticides:
   - Weedicides:
   - Fungicides:

23. How many litres of pesticides do you apply to your crops in a season?
   - Insecticides:
   - Weedicides:
   - Fungicides:

24. What is the average duration of each application?
   - Insecticides:
   - Weedicides:
   - Fungicides:

25. What is the size of farm area you usually spray?

SECTION C: FARM ACTIVITIES AND PESTICIDE APPLICATION
SECTION D: OCCUPATIONAL SAFETY

25. Have you received any training or instructions on pesticide safety?
   □ Yes
   □ No

26. If yes, where did you obtain your training or instructions?(Tick all that applies)
   □ Agricultural Extension/Technical Officers
   □ Pesticide Sales Agent
   □ Television
   □ Radio
   □ Newspaper
   □ Colleague Farmer
   □ Family Members
   □ Others(specify)__________

27. Do you read and understand the instruction labels on pesticides before using it
   □ Most times
   □ Sometimes
   □ Never

28. Can pesticides harm human health?
   □ Yes
   □ No

29. Can pesticides harm the environment?
   □ Yes
   □ No

30. Can pesticides enter human body through the:
   Skin? Yes_______ No_______
   Nose? Yes_______ No_______
   Mouth? Yes_______ No_______

31. Which part of the body is the most common route of pesticide exposure among farmers?
   □ Mouth
   □ Nose
   □ Skin

32. How long does it take for you to re-enter your farm after spraying?_____________________

33. Do you suck or blow the nozzle of your spraying equipment when it is blocked?
   □ Most times
   □ Sometimes
   □ Never

34. Do you accidentally spill pesticides on your body or cloth during mixing, loading or applying pesticides?
   □ Most times
   □ Sometimes
   □ Never

35. What do you wear to protect yourself when mixing and loading pesticides? (Tick all that apply)
   □ Hand gloves
   □ Overalls
   □ Rubber boots
   □ Nose mask
   □ Respirators
   □ Long sleeve shirt
   □ Short sleeve shirt
   □ Trousers
   □ Knicker(shorts)
   □ Head cap/scuff/hat
   □ Goggles/safety glasses
   □ Apron
   □ Others(specify)_____________ _______
36. What do you wear to protect yourself when applying pesticides?
   - Hand gloves
   - Overalls
   - Rubber boots
   - Nose mask
   - Respirators
   - Long sleeve shirt
   - Short sleeve shirt
   - Trousers
   - Knicker (shorts)
   - Head cap/scuff/hat
   - Goggles/safety glasses
   - Apron
   - Others (specify) ________

37. What do you wear to protect yourself when cleaning/washing of spraying equipment?
   - Hand gloves
   - Overalls
   - Rubber boots
   - Nose mask
   - Respirators
   - Long sleeve shirt
   - Short sleeve shirt
   - Trousers
   - Knicker (shorts)
   - Head cap/scuff/hat
   - Goggles/safety glasses
   - Apron
   - Others (specify) ________

38. After pesticide spraying, do you carry any child, wearing your farm clothes?
   - Most times
   - Sometimes
   - Never

39. After pesticide spraying activities, do you take complete shower immediately?
   - Most times
   - Sometimes
   - Never

40. After pesticide spraying activities, where do you shower?
   - At farm
   - At home
   - Others (specify) ________

41. Do you wash your farm clothes after spraying before the next use?
   - Most times
   - Sometimes
   - Never

42. Where do you wash your farm clothing?
   - At the farm
   - At home
   - Others (specify) ________

43. Do you change your clothes after spraying before going home?
   - Most times
   - Sometimes
   - Never

44. Do you drink/eat/chew anything during mixing, loading, or application of pesticides?
   - Most times
   - Sometimes
   - Never
Additional Notes

Investigator: Albert Atabila

Organization:

School of Environment
Griffith University
Queensland, Australia
Appendix 4: Field Observation Guide (Check-List)

Centre for Environment and Population Health (CEPH)

Field Observation Guide
(For observing farmers before, during, and after spraying insecticides)

ID: ____________  No. Name of Recorder: ________________

Today’s date: ______/_____/______  Observation Start:_______End________
  Day    Month    Year

1. Name of Farmer/Applicator:

2. Description of farm:

3. Description of insecticide used:
   a. Trade name:
   b. Formulation:
   c. Manufacturer:
   d. Expiration date:
   e. A label describing the product and instructions for use: YES/NO
   f. A label describing the

5. Where were pesticides stored?
   ☐ Residential premises
   ☐ On the farm
   ☐ Other place(specify)

6. List of preparatory activities

________________________
________________________
________________________

7. What type of spraying equipment was used?
   ☐ Hand-pressurized backpack
   ☐ Motor-pressurized backpack
   ☐ Other equipment(specify)

8. Was any PPE used during mixing, loading, and application of insecticide?(tick)
   ☐ Yes
   ☐ No

9. If yes to 7, what type of PPE was used?(tick)
   ☐ Overall
   ☐ Hand gloves

253
### Instructions for Use: YES/NO

4. Distance of pesticide application site from farmer’s residence:

<table>
<thead>
<tr>
<th>Rubber boot</th>
<th>Slippers</th>
<th>Safety glasses/goggles</th>
<th>Nose masks</th>
<th>Respirator</th>
<th>Head cap/scuff/hat</th>
<th>Apron</th>
<th>Others (specify)</th>
</tr>
</thead>
</table>

10. What type of clothing was worn by farmer during application? (if not an overall)

- Short sleeve shirt
- Long sleeve shirt
- Long pants
- Short pants

11. What was the duration of the insecticide application?

12. Was there any leakage from the nozzle or any part of the spraying equipment?

- Yes
- No

13. Was there any incidence of spill/splash on the skin/cloth of farmer during mixing, loading, mounting of equipment or spraying? (tick)

- Yes
- No

14. What tasks were performed by farmer? (tick)

- Mixing of insecticides
- Loading of insecticides
- Application of insecticide
- Washing of spraying equipment
- Others (specify) ________________________________

15. Did farmer wash his/her hands or body immediately after spraying?

- Yes

20. Weather condition

- Temperature: Hot_____Warm______
- Cold____
- Wind: Windy_____Calm______
- Sun: Sunny_____Cloudy______
- Humidity: Humid_____Not humid_

21. Was the spraying done against the wind direction?

- Yes
- No

22. What time of the day was spraying done?

- Morning
- Afternoon
- Evening

23. Was spraying equipment washed after spraying?

- Yes
- No

24. How were empty insecticide containers disposed of?

- Left on the farm
- Buried in the ground
- Other means (specify)

25. How was left over pesticides disposed of?

26. Was any child (below 15 years) present during mixing, loading, spraying period?

- Yes
- No

27. Did any child (below 15 years) participate in the mixing, spraying, and application of the insecticide?

- Yes
- No
<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>16. Did farmer drink/smoke/or chew during mixing, loading, spraying period?</td>
<td>Yes</td>
</tr>
<tr>
<td>17. What was the total size of farm area sprayed during the day?</td>
<td>__________</td>
</tr>
<tr>
<td>18. How much insecticide was applied during the day?</td>
<td>_____________</td>
</tr>
<tr>
<td>19. What was the concentration/dilution of the insecticide applied?</td>
<td>_____________</td>
</tr>
</tbody>
</table>

28. If yes to 24 and 25, note details of child/children

**Additional Notes**

____________________________________________________________________________________________________
____________________________________________________________________________________________________
____________________________________________________________________________________________________
____________________________________________________________________________________________________
____________________________________________________________________________________________________

**Investigator:** Albert Atabila

**Organization:**

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Queensland, Australia
REFERENCES


Ansa-Asare, O. D., Darko, H. & Obiri, S. 2015. Assessment of Carcinogenic Risk and Non-Carcinogenic Health Hazard from Exposure to Toxicants in Water from the


Environmental and Health Effects of Termiticides under Australian Conditions. 
*Environmental Health*, 3, 29-58.


