KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY,
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FACULTY OF BIOSCIENCES
DEPARTMENT OF THEORITICAL AND APPLIED BIOLOGY

A STUDY OF THE EFFECTS OF CHEMICALS USED TO CONTROL DISEASES AND PESTS OF COCOA ON THE USERS. A CASE STUDY OF ATWIMA NWABIAGYA DISTRICT.

A THESIS SUBMITTED TO THE DEPARTMENT OF THEORITICAL AND APPLIED BIOLOGY, FACULTY OF SCIENCE, KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KUMASI IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF SCIENCE (ENVIRONMENTAL SCIENCE)

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DECLARATION

I hereby declare that, this thesis presented to the Department of Theoretical and Applied Biology, in partial fulfillment for the award of MSc. Degree, is true account of the student's own work except for the references which have been duly acknowledged.

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Glossary

Aerosols – Solid or liquid particles suspended in a gas or particulate matter in an exposure / gaseous medium

Ppm - Parts per Million

LC50 – the medium concentration to which animals are exposed for a specified time that will kill 50% of the animals within a fixed period of time after

NOEL – No Observable Effect Level

NOAEL – No Observable Adverse Effect Level

CSSVD – Cocoa Swollen Shoot Virus Disease

CODAPEC – Cocoa Diseases and Pests Control

COCOBOD – Cocoa Board

FAO – Food and Agriculture Organization

WHO – World Health Organization

JMPR – Joint FAO / WHO Meeting on Pesticide

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Abstract

In Ghana, periods of higher producer prices of cocoa beans have witnessed a corresponding increase in production. This has led to a significant increase in the use of various chemicals by our farmers in their attempts to boost production. There are however very scanty information on the toxicity of these chemicals on the health of the non – target organisms. This study was undertaken to access the effects of these chemicals on the health of the users within the Atwima Nwabiagya district in the Ashanti region of Ghana.

The study consisted of a questionnaire survey and laboratory experiment using albino rats. Questionnaire was administered by the interviewer to 100 respondents who were selected from five different centers within the district, thus ensuring a wide representation. The laboratory experiment consisted of 4 groups (6 rats per group). Three of the groups were exposed for 8 weeks to different concentrations of chemicals commonly used by farmers whilst the other group was set up as control. Rats were sacrificed at the end of the exposure period and histopathology of targeted organs carried out.

Results from the questionnaire survey indicated that the chemicals could cause dermal diseases such as skin rashes and irritations to the users. Laboratory experiment also indicated that the chemicals could be toxic to the exposed rats if the concentrations of the chemicals are high enough. Rats exposed to high concentrations of both chemicals used for the experiment (bifenthrin and thiamethoxam) were significantly of smaller body weights ($p \leq 0.05$) compared with the control rats.

The lungs of the rats exposed to high concentration of thiamethoxam were the slightly affected organs, but no signs of toxicity were observed on the other organs (hearts, liver, kidneys) of rats exposed to the other concentrations including bifenthrin. Furs of rats were also affected.

1.0 GENERAL OVERVIEW AND INTRODUCTION

1.1 Introduction

Cocoa originated from the lower Amazon of Brazil and was brought to Ghana from Fernando Po in 1879 and from Sao Tome in the 1880's (Opoku *et al*., 1998).The first recorded export of beans from Ghana was in 1891 and since then, cocoa has been the main export crop and a major source of foreign exchange and domestic income earner. Until 1977, and for 66 years (1910 to 1977), Ghana was the world's leading of cocoa producer with the market shares ranging from producer 30-40% of the world's total production (Bateman, 1988). Records indicate that production increased from a level of 36.3 metric tonnes in 1891 to an all time peak of about 557,000 metric tonnes in 1964/65 giving Ghana a global output share of about 33% and the leading cocoa producer (Opoku *et al*., 1998). Thereafter, production continued to drop and reached the lowest level of 158,956.00 metric tonnes in 1983/84, which constituted about 9% of world's production. Consequently, Ghana lost her position as the world's number one producer (Gill and Duffus, 1989).

The decline in cocoa production in Ghana raised a great deal of concern and in 1995, a high-powered committee chaired by a Deputy Minister and comprising executives of the Ghana Cocoa Board, Ministries of Agriculture and Finance and other high-ranking government officials and farmers' representatives, was charged with conducting a rapid rural appraisal of the cocoa industry to identify the constraints to production and recommend measures for solving the problems with the view to arresting the decline in production (Anon.,1995). General and more localized studies identified several technical factors which contributed to the dwindled cocoa production levels in Ghana, (Anon., 1990; Freud *et al*., in press). Paramount among these are the ravages caused by cocoa capsids

(*Heteroptera Siridae*) and diseases such as swollen shoot caused by cocoa swollen shoot virus and black pod caused by the fungi Phytophthora palmivora and P. megakarya.

As part of efforts to arrest the decline in cocoa production, the Government of Ghana through Cocoa Board initiated a National Cocoa Diseases and Pest Control (CODAPEC) programme in 2001/02 cocoa season, popularly known as "Mass Spraying" to assist all cocoa farmers in the country to combat the Capsid/Mirid and the Black Pod disease. Mass Spraying is a farm management by COCOBOD where array of chemicals are used to prevent or control pests and diseases causing organisms with the aim to increase yield. This is done on several farm holdings belonging to independent holders or farmers without any direct cost to the farmers. The spraying exercise is done irrespective of their political or religious inclinations. Other objectives were to train farmers and technical personnel on the cultural and chemical methods of pests and diseases control, educate and train local sprayers on safe pesticides usage, help put more money in the pockets of farmers and create jobs for the unemployed youth in the rural communities (Dormon, 2006).

The CODAPEC programme has been very productive. The programme is a source of employment for the youth. CODAPEC alone has engaged over 60,000 people as sprayers, supervisors and mechanics in the rural communities (Dormon, 2006). Several transporters and Distributors are directly and indirectly involved in the spraying exercise.

As a result of the CODAPEC programme, the black pod disease incidence and mirid infestation have reduced significantly as shown by field evidence and by farmers' testimonies. Hitherto, loses due to black pod were about 60 to 100% whilst losses due to mirid were between 25% and 35%. Production figures show that yield per ha has increased

substantially in virtually all the districts across the country. Consequently, cocoa production in Ghana has gone up from 380,000 metric tonnes at the inception of the programme to almost 500,000 metric tonnes in 2002/2003 and reached an all time high of 740,458 metric tonnes in the 2005/2006. It is worthy to mention that the introduction of a "mass spraying" exercise between 1959 and 1962 is believed to have resulted in the high production of over 580,000 metric tonnes recorded in the 1964/65 season. Farmers own testimonies strongly suggest that their financial positions have generally improved. CODAPEC has helped to generate more foreign exchange for the country through cocoa sales.

The renewed enthusiasm of the farmers following the introduction of CODAPEC has rekindled cocoa cultivation; new farms have been established and old ones rehabilitated. According to the Seed Production Unit of COCOBOD, the demand for planting materials has gone up substantially since the programme begun some nine years ago. The programme has demonstrated beyond doubt that Cocoa farming can be profitable.

As a result, chemicals have become an indispensable part of human life, sustaining activities and development, preventing and controlling many diseases, and increasing agricultural productivity. Despite their benefits, chemicals may cause adverse effects on animals and human health (IPCS, 2001).

Recent years have seen increasing awareness and global concern over the quality of the environment and the potential dangers associated with lack of environmental and

hazardous chemicals management. Due to the enormous use of pesticides as a result of the introduction of CODAPEC, many animals in our environment including the farmers are frequently exposed to its associated risk effects.

The incidence of work and environment-related illnesses in human beings in the world including Ghana is increasing. Farmers appear to encounter many serious occupational health and safety problems that health professionals have to manage. Unfortunately, there are very few trained occupational safety and health personnel who can manage and treat occupational related illnesses (OEHU, 2002).

In addition, most of the farmers, least observe health and safety measures in the use and handling of these chemicals. They seldom use protective equipment due to their ignorance of the health effects or risks associated with the use and handling of these chemicals, negligence, unavailability and high cost of protective equipment. The risks and potential health hazards that these farmers are likely to be exposed to are very high, either in the short term or long term. Occupational health hazards to farmers involved in frequent spraying with these chemicals include dermatitis and various lung diseases ranging from acute irritation to chronic bronchitis and occupational asthma. In more acute exposure, death can also result (IARC, 1991).

1.2 Justification

The various health effects associated with the usage of synthetic chemicals used for spraying on cocoa farms have been clearly established by research in the developed countries. But in Ghana however, this problem has not been given much attention. This is the country where synthetic chemicals used have been intensified by the government and

the farmers through the introduction of the CODAPEC programme, and yet very scanty information on the toxicity of these chemicals to the users is available.

There is increasing evidence that farmers in the study area are suffering from various symptoms of chemical poisoning, particularly the cocoa farmers who are always exposed to various synthetic chemicals. Most of these farmers have poor understanding of the basic principles underlying the risks of pesticides to human, such as observance of personal hygiene, first aid, techniques of application, handling and disposal of empty containers and other environmental issues (www.eduwhere.com/c, 08/07/2010).

The study area was selected because of a long history of cocoa production and it is the area where the government strategy to increase cocoa production (CODAPEC) is intensified. It is therefore expected that, the information and experience which has been gathered from this rich site could be used as a guide for study of other cocoa production areas in Ghana and the rest of the world so as to help educate people, particularly our farmers about the best way to control pests and diseases in the farms with no or minimal health and environmental adverse effects. It is against this background that the present study seeks to assess the effects of these chemicals on the health of the users in the Atwima Nwabiagya district of Ashanti region.

1.3 Objectives of the study

The study sought to determine the effect of some of the chemicals for spraying of cocoa farms on the health of the users;

Specifically the following objectives were considered:

1. The types of chemicals used.
2. The concentrations normally used.

3. To evaluate the effects of the chemicals on the health of the animals in the environment.

2.0 LITERATURE REVIEW

Animals are exposed to a number of hazards in the environment. And for this reason much concern should be given to the observance of environmental health precautions as well as safety measures. Most chemicals used for spraying are classified as hazardous substances because they contain potentially harmful ingredients (WHOPES, 2005).

Exposure to these chemicals can cause injury and illness through inhalation of the toxic aerosols and mists, or absorption of irritants through the skin. These hazardous substances encountered in spray include pyrethroids (bifenthrin), thiamethoxam and imidacloprid (Dormon, 2006). Many cocoa farmers spray their farms for at least three times in a year and this exposes most animals including humans to various hazardous chemicals.

2.1 ROUTES OF EXPOSURE TO CHEMICALS USED

The spraying on cocoa farms results in increased exposure to hazardous substances. The main route of entry of these hazardous substances into the body is generally through inhalation of aerosols (Engstrom *et al*., 1978).

Inhalation and percutaneous absorption are the primary routes of solvent uptake into peripheral blood, which begins within minutes of the onset of exposure (WHO 1985). The principal route is uptake by inhalation and depends on the following: solvent concentration in inhaled air, blood/air partition coefficient of the solvent, alveolar ventilation rate, blood perfusion of lungs, and duration of exposure (Astrand1975; WHO 1985).

2.1.1 Dermal or Skin Exposure

The animal skin is not very permeable and therefore, is a relatively good lipoid barrier separating animals from the environment. However, some chemicals can be absorbed by the skin in sufficient quantities to produce systemic effects e.g., various chemicals have caused the death in agricultural workers and some environmental animals after absorption through the intact skin (Fischman 1991).

Uptake of chemicals through the skin depends on duration of contact, skin thickness and perfusion, degree of hydration and the presence of cuts abrasions, or skin diseases (Riihimaki and Pfaffli 1978; Bird 1981). Dermal exposure to hazardous substances is known to cause a variety of diseases including skin cancer and dermatitis. There are many chemicals (e.g. polycyclic aromatic hydrocarbons and some solvents).

2.1.2 Ingestion

Potential exposure exists through swallowing (WHOPES, 2005).many environmental chemicals enter the food chain and are absorbed from the gastrointestinal tract. Poisons within the gastrointestinal tract do not produce injury to the individual until they are absorbed.

With control strategies reducing inhalation and skin exposures, the relative contribution from the ingestion route may be increasing (DEOM, 2001).

2.2 SOLVENT TOXICITY

Exposure to hazardous chemicals used in spray on cocoa farms can have serious health effects on animals in our environment including humans if not controlled. This makes the handlings of these hazardous chemicals difficult which require great care by the users so as to avoid exposure through environmental contamination.

2.2.1 Acute Toxicity

Acute toxicity is the one caused by a single (short term) exposure or multiples within the short time period which cause immediate health crises. An acute effect is generally regarded as an effect that occurs within the few days after exposure, usually less than two weeks.

Several experimental animal studies have been conducted to determine their acute neurotoxic effects on the central nervous system rather than the potential chronic neurotoxic effects from long-term exposure. The acute toxic effects of solvent inhalation noted in animals reflect those seen in humans – that is, narcosis, anaesthesia, respiratory arrest, unconsciousness, central nervous system depression, and death (Browning, 1965) Short-term effects also include irritant contact dermatitis, headaches, dizziness, nausea, fatigue, vomiting, diarrhoea, nose, throat and lung irritation and burns to the skin or eyes (Browning, 1965).

2.2.2 Chronic Toxicity

Chronic toxicity and effects are long lasting and can result from either a single exposure or multiple exposures. Chronic toxic substances are by far the most difficult for society to cope with because their effects are subtle and long ranging, making it difficult to determine

their impact on humans and living organisms. Two important examples of chronic toxic substances are carcinogens and teratogens.

Among the long term health effects associated with exposure to spray chemicals include lung cancer, allergic contact dermatitis, occupational asthma, damage to reproductive system, kidney or liver damage (Browning, 1965).

2.3 HEALTH EFFECTS

2.3.1 Respiratory Effects

Acute and chronic health effects often result from exposure to hazardous substances among which the short-term effects include respiratory tract irritation, shortness of breath, dizziness, tightness of the chest, nausea and headaches. Long term effects may include lung cancer, asthma, sensitization of the respiratory system, abnormal reduction in lung function as well as central nervous system dysfunction (Browning, 1965).

Solvent inhalation by animals may cause effects ranging from an alcohol like intoxication to narcosis and death from respiratory failure, with a spectrum of intermediate symptoms that include drowsiness, headache, dizziness, dyspepsia and nausea (Browning, 1965).

2.3.2 Skin / Dermal Effects

Exposure of the skin and eyes to hazardous substances may result from the presence of airborne spray mist (aerosol) through direct contact. Health effects usually associated with these kinds of exposures may be acute burning of the eyes, skin contact with chemicals may result in acute irritant dermatitis, chronic allergic contact dermatitis or defattening of the skin (Leffler, 1999).

2.4 EFFECTS OF THE CHEMICALS USED FOR SPRAY

2.4.1 Akate Master (Bifenthrin)

Bifenthrin is a pyrethroid containing aromatic hydrocarbons (which are also known as synthetic pyrethroids) are insecticides chemically similar to pyrethrins found in natural pyrethrum extracted from the flowers of chrysanthemum, known for centuries for their insecticidal activity (WHO, 1999). There are two types of pyrethroids that differ in chemical structure and symptoms of exposure. Type 1 pyrethroids include allethrin, tetramethrin, resmethrin, d-phenothrin, bioresmethrin and permethrin (1 & 2). Some examples of types 2 pyrethroids are cypermethrin, cyfluthrin, deltamethrin, cyphenothrin, fenvalerate, and fluvalinate (1 & 2). Both type 1 and 2 pyrethroids inhibit the nervous system of insects. This occurs at the sodium ion channels in the nervous membrane.

The toxicity of bifenthrin (synthetic pyrethroid) in animals and other mammals like humans is caused by similar mechanisms as the insecticidal activity, so these properties are usually correlated. The marked differences in the toxicity of bifenthrin to insects (target organisms) and animals are apparently caused by differences mainly in the voltage-sensitive sodium channels (Soderlund *et al*., 2002).

Repeated oral doses to rats for 7 days induce axonal degeneration to the sciatic nerve. Degeneration, however, occurs only with doses high enough to cause death in some other treated rats (Aldridge, 1990).

Bifenthrin was tested for carcinogenicity in rats and mice and did not show carcinogenic potential in rats, but an increased incidence of submucosal urinary bladder haemangioma was observed in males at the highest dose; the NOAEL for carcinogenicity was 10 times higher than that for neurotoxicity. JMPR considered that a carcinogenic activity of bifenthrin cannot be excluded but, considering the negative genotoxicity, bifenthrin is unlikely to cause a carcinogenic hazard to mammals (IPCS, 1993).

While a wide range of genotoxicity tests were negative for bifenthrin, positive results have been reported for the mouse lymphoma assay in one of two studies, and for unscheduled DNA synthesis (UDS) in rats (slightly positive at a high dose level; IPCS, 1993).

Since the nervous system is the target of bifenthrin toxicity, several acute and subchronic neurotoxicity studies have been conducted on pyrethroids such as bifenthrin, permethrin, cyfluthrin.

In acute oral neurotoxicity studies the effects of pyrethroids were transient and were observed at doses from 10mg/kg to 300mg/kg within 1-14 days after treatment. In sub chronic neurotoxicity studies that involved dietary exposure for 13 weeks, the signs of pyrethroid (bifenthrin) intoxication were observed at doses ranging from 29 mg/kg to 170mg/kg; they generally persisted, but did not worsen, with continued treatment beyond 4 weeks of exposure (Soderlund *et al*., 2002).

Signs of neurological toxicity have been noted in the acute toxicity studies for determining the LD50 for either technical bifenthrin or its formulations. A single oral dose of 20mg/kg

technical grade (91.4% purity) bifenthrin, or 18.3mg/kg bifenhrin, resulted in tremors in 6 of the 10 rats, as early as 3 hours after dosing (Freeman, 1982).tremors, chromorhinorrhea, chronic convulsions and death occurred in rats that were treated with 150mg/kg FMC 548002EC which contained 26.5% bifenthrin, or 39.8mg/kg bifenthrin. The same neurotoxicity signs were observed with a single oral dosing of 500mg/kg Talstar 80 G/L Flowable which contained 8% bifenthrin, or 40mg/kg bifenthrin.

The current database on clinical observations shows consistency in the NOEL determined from oral galvage and feeding studies. A NOEL of 1mg/kg/day was established from a tetratology study through oral galvage. The NOEL was based on tremors observed in 18 of 25 pregnant rats (starting day 4 of exposure) at the next higher dose of 2.0mg/kg/day (DeProspo, 1984e). An acute NOEL can also be determined from two feeding studies: a chronic toxicity by McCarty (1986) and a 90-days toxicity study by Rand (1984). In both of these studies, tremors were observed in rats starting on day 3 of consuming diets that contained 100ppm bifenthrin (5mg/kg/day) and starting on day 2 at 200ppm bifenthrin (10mg/kg/day). Based on tremors, the acute NOEL from these two studies was 50ppm in the diet (2.5mg/kg/day). The NOELs from these three studies differed by 2.5-fold. The lowest NOEL of 1mg/kg/day was used in 1991 to characterize the risk of acute exposures (Reed, 1991).

Physiological and neurochemical studies of pyrethroid-intoxicated animals confirm that acute pyrethroid intoxication is associated with altered nerve functions; principally involving neuroexcitatory effects in the brain, spinal cord peripheral nervous system.(Soderlund *et al*., 2002).

Occupational exposure to bifenthrin may occur through dermal contact and inhalation of dust and sprays. While inhalation is the main route of exposure in workers applying the compounds in agriculture or workplaces where bifenthrin is produced or used (IPCS, 1990). Workers in a bifenthrin-manufacturing plant reported mild and temporary paresthaesia (skin tingling) resulting from skin contact. Of emergency calls received by the manufacturer during 2002 from individuals applying products containing bifenthrin, the most common complaints were dermal sensations of burning/tingling and eye irritation, which mostly resolved within 24 hours. The meeting concluded that the existing database on bifenthrin was adequate to characterize the potential hazards to fetuses, infants and children.

Exposure of the general population may occur by inhalation, skin contact with product, by eating food containing residues of pyrethroids applied as pesticides or veterinary drugs, or through accidental swallowing or drinking of pyrethroids products. Recent studies carried out in the European Union and the United States have shown detectable amount of pyrethroid metabolites in urine samples from the general population (Schettgen *et al*,. 2002; Baker *et al*,. 2001).

Symptomatic acute cases generally follow accidental overexposure or lack of care in handling the compounds at the workplace, whereas accidental ingestion of high doses is the main cause of poisonings for the general population.

Acute poisoning very rarely poses a life-threatening risk to the exposed subject, but severe poisonings and even potential for causing mortality may arise if concentrated formulations are swallowed (Hayes, 1982; Bateman, 2000).

In occupational poisonings, the initial symptoms are skin burning, itching or dizziness. These sensations reported in exposed subjects might not be the result of skin reactions, but signs of peripheral nerve involvement (He *et al*., 1988,) About half of the occupational patients develop abnormal facial sensitization (paraesthesia); in the case of swallowing, the main symptoms are epigastric pain, nausea, and vomiting (He *et al*., 1989).

The systemic systems include dizziness, headache, nausea, anorexia and fatique and, in the most severe cases, fasciculation in large muscles of the extremities. The nervous system is the target organ of the toxic action of pyrethroids, but the effects on the respiratory tract can also be observed, such as massive haemorrhages and oedema of the lungs following inhalation at concentrations above or near lethal concentrations (Soderlund *et al*., 2002).

Muller-Mohnssen recently reported a case series of subjective symptoms in people with preceding exposure to pyrethroids. The most frequently observed changes were: cerebro-organic disorders, such as reduced intellectual performance, and personality disorders, sensory and motor polyneuropathy, frequently in the lower legs, and vegetative disorders (Muller-Mohnssen, 1999).

Similarly, to what was observed in animals, a transient irritation was also observed in human volunteers exposed for a 1-hour period to pyrethroid (cyfluthrin) at concentrations of approximately 0.1mg/m3; exposures to 0.2mg/m3 induced marked irritation (Pauluhn & Machemer, 1998).

Itching, pricking sensations, numbness, burning of the skin and the eyes or tingling of the skin are the symptoms most commonly reported after contact with pyrethroids (Le Quesne *et al*., 1980; Tucker & Flannigan, 1983; Kolmodin-Hedman, 1982; He *et al*., 1988; Chen *et al*., 1991). Symptoms usually start 1-6 hours after exposure (Kolmodin-Hedman, 1982; He *et al*., 1989; Zhang *et al*., 1991) and last not more than 24hours, but in some cases they may last up to 3 days.

2.4.2 Confidor (imidacloprid)

Imidacloprid is a nicotinoid neutoxin that acts by irreversibly blocking acetylcholine receptors. Both mammals (animals) and insects have acetylcholine receptors that can be blocked by imidacloprid. Symptoms of imidacloprid poisoning include staggering, trembling, immobility and lethargy.

Imidacloprid's low vapour pressure results in a very low potential for volatilization. Therefore, imidacloprid is most likely to be found in air during and immediately after spraying on crops, where it will exist primarily as an aerosol.

Canadian livestock may be exposed to pesticide residues through consumption of contaminated feed/crops, or through ingestion of contaminated water. Imidacloprid is rapidly absorbed from the gastrointestinal tract and within 48 hours of administration is

effectively eliminated through urine (70 to 80%) and feces (20 to 30%) (Tomlin, 1994;PMRA. 2001). In mammalian systems, imidacloprid is hydroxylated and hydrolyzed to the critical metabolic product, 6-chloronicotinic acid. This metabolite is further conjugated and eliminated or reduced to guanidine (Tomlin 2000).

Imidacloprid is moderately toxic to animals via the oral route of exposure (PMRA 2001). Acute toxicity of imidacloprid to rats varies, depending on the route of exposure, with oral dosing posing the greatest toxic threat (Mulye 1996). The oral LD_{50}s for rats exposed to one dose of technical-grade imidacloprid was 424 mg a.i./kg bw for males and 450 – 475 mg a.i./kg bw for females (Mulye 1996). The symptoms of acute toxicity to domestic animals resemble a general nicotine-like response: fatigue, twitching, cramps, and muscle weakness (Hovda and Hooser 2002). In rats, oral exposure induced apathy, respiratory disturbances, decreased motility, staggering gait, narrowed palpebral fissures, transient trembling and spasms, which subsided in under one week (Mulye 1996). The thyroid appears to be a target organ in imidacloprid dosing, as thyroid lesions are associated with high doses in short-term and chronic feeding studies of imidacloprid (Hovda and Hooser 2002). In a two-year rat study, the oral NOAEL for thyroid toxicity was determined to be 100 mg a.i./kg diet (i.e., 5.7 mg a.i./kg bw/day for males and 7.6 mg a.i./kg bw/day for females), with a LOAEL of 300 mg a.i./kg diet (i.e., 16.9 mg a.i./kg bw/day for males and 24.9 mg a.i./kg bw/day for females) (U.S. EPA 1995).

The U.S. EPA (1994) considers imidacloprid to be a non-genotoxic chemical to mammals. Imidacloprid has been classified as a ‘Group E’ chemical, one for which no evidence of

Imidacloprid carcinogenicity exists (U.S. EPA 1995). Tomlin (2000), states that it is neither mutagenic nor teratogenic. A 2-year mouse study observed no carcinogenic effects and determined a NOAEL of 1,000 mg a.i./kg diet for non-carcinogenic effects such as decreased body weight, food consumption, water intake, and liver and spleen weight (PMRA 1995). The U.S. EPA (1995) reports that no carcinogenic effects were observed in a 2-year study, in which rats were fed imidacloprid at doses as high as 1,800 mg a.i./kg. With a NOEL reported for oncogenicity in rodents at 208 mg a.i./kg bw/day, PMRA suggests there is no evidence for oncogenicity in rodents (reviewed in Mulye 1996).

EXTOXNET (1998) lists imidacloprid as weakly mutagenic, based on 2 positives in a series of 23 mutagenic assays submitted to the U.S. EPA for registration. The first positive assay tested for chromosome aberrations in an *in vitro* cytogenetic study with human lymphocytes as a result of imidacloprid exposure (U.S. EPA 1995). The second assay measured positive cytogenotoxicity in Chinese hamster ovary cells (U.S. EPA 1995). A subsequent study by Shah et al. (1997) also provides a contradictory assessment of the genotoxic potential of imidacloprid. This study used a ^{32}P-postlabelling assay to detect the presence of DNA adducts in calf thymus DNA that were exposed to the insecticide. The presence of DNA adducts, the covalent binding of DNA to a particular chemical, is the well-established cause of genotoxicity and the initial event in the process of carcinogenesis. Therefore, the assay is a direct measure of the genotoxic potential of a chemical. This study used Admire, the end use product of imidacloprid and reported significant adduct formation for this chemical, relative to controls. Although, this study did not use the pure chemical imidacloprid, this result merits further investigation.

In a reproductive study on both rats and chinchilla rabbits, imidacloprid was administered to pregnant females through gavage on gestation days 6 to 15 for the rat and 6 to 18 for the rabbit (PMRA 1995). The study reported no developmental effects on the fetuses at 30 mg a.i./kg bw/day and 24 mg a.i./kg bw/day in the rat and rabbit, respectively. Skeletal abnormalities were observed at higher doses, with LOAELs of 100 and 72 mg a.i,/kg bw/day for the rat and rabbit, respectively (PMRA 1995). Effects on maternal body weight gain (and maternal food consumption, in the case of rabbits) were observed at lower concentrations, with LOAELs of 30 and 24 mg a.i./kg bw/day for the rat and rabbit, respectively. The compound is not considered teratogenic for either species (Mulye 1996).

In a rat reproductive study with dietary administration of imidacloprid using two generations, each with two litters, the parental NOEC was 250 mg a.i./kg diet (PMRA 1995). At a dietary concentration of 700 mg a.i./kg (i.e., 47.3-56.7 mg a.i./kg bw/day for males and 52.3-62.8 mg a.i./kg bw/day for females), decreased weight gain was observed in the parents. Similarly, effects on pup body weight were observed at 700 mg a.i./kg diet; however, no reproductive effects were observed at this concentration (PMRA 1995). Imidacloprid exhibits low toxicity via the dermal route of exposure (PMRA 2001). The LD_{50} for dermal application of imidacloprid to rats was reported as >5000 mg a.i./kg bw (Mulye 1996). A dermal rat LD_{50} of >2000 mg a.i./kg bw has been reported for an end-use product containing imidacloprid, Admire 240F (Mulye 1996). Female rats suffered reduced gain in body weight with dermal exposure, which was the only sign of toxicity (reviewed in Mulye 1996). Imidacloprid is not considered an irritant to rabbit skin and eye, and is not a skin sensitizer in guinea pigs (Mulye 1996).

Imidacloprid exhibits low toxicity via the inhalation route of exposure (PMRA 2001). The inhalation 4-h LC_{50} for rats was reported as >0.069 mg a.i./L air (as aerosol) and >5.3 mg a.i./L air (as dust) (Mulye 1996). Signs in rats exposed through inhalation to imidacloprid included slightly laboured breathing, decreased motility, piloerection, slight tremor and decreased body-weight gain (Mulye 1996). Rats exposed to imidacloprid through inhalation for 6 hours/day, 5 days/week for 4 weeks showed increased liver weight, increased coagulation time, and clinical chemistry changes at an exposure rate of 0.191 mg a.i./L air/day (i.e., 51.9 mg a.i./kg bw/day) (PMRA 1995).

Systemic toxicity associated with imidacloprid exposure was not observed in rabbits repeatedly exposed via skin over 21 days, or in dogs repeatedly exposed to oral doses of technical compound over 52 weeks (PMRA 1995; Mulye 1996). For these studies, toxicity endpoints were a NOEL of >1000 mg a.i./kg bw/day for the rabbit and >72 mg a.i./kg bw/day for the dog (Mulye 1996). However, in another study, dogs exposed to imidacloprid in their diet for 13 weeks at a concentration of 600 mg a.i./kg diet (i.e., 22.1 mg a.i./kg bw/day for males and 24.8 mg a.i./kg bw/day for females) exhibited signs of trembling and emaciation (PMRA 1995).

2.4.3 Actara (Thiamethoxam)

Thiamethoxam is a neonicotinoid insecticide that has been extensively tested in animal models for short- and long-term toxicological effects. An increased incidence of liver tumours was seen in male and female Tif:MAGf mice when fed in the diet for 18 months at concentrations up to 2500 ppm. In marked contrast, there were no increases in cancer incidences either in the liver, or at any other site, in rats fed on diets containing up to 3000 ppm thiamethoxam for 2 years. Furthermore, thiamethoxam was not genotoxic. Previous

papers in this series reported the development of a mode of action for the mousespecific liver tumorigenesis (Green *et al.*, 2005a), as well as an explanation for the species differences in response and metabolism between the rat and the mouse and the significance of these species differences to human health (Green *et al.*, 2005b*)*. Given that a well-defined mode of action can be described for the thiamethoxam-related mouse liver tumors, the purpose of this paper is to describe the systematic evaluation of the relevance of these tumors to human health.

This evaluation has been prepared according to EPA's Guidelines for Cancer Risk Assessment (U.S. EPA, 1999) and according to methods laid out in the International Life Sciences/Risk Sciences Institute (ILSI-RSI) publication (Cohen *et al.* 2003; Meek, *et al.* 2003; and Cohen, *et al.* 2004). This methodology provides a decision-logic based approach to determining the relevance to humans of a compound-related increased cancer incidence in animal studies. Both the EPA and the ILSI-RSI documents rely on similar systematic thinking to arrive at a justifiable position. Downloaded from toxsci.oxfordjournals.org by guest on February 2, 2011 - 5 - The process used here and proposed by ILSI-RSI as a framework for determining the human relevance of rodent tumors, asks a series of questions that guides thinking concerning the significance of findings to human health. The first question is whether or not there are sufficient data to describe a mode of action that is comprised of demonstrable key events. The essence of a full, weight-of-evidence data evaluation relies on a systematic consideration of criteria that either strengthens or weakens a postulated mode of action and the underlying key events. The Hill criteria (Hill, 1965) for causation serve as a general guide. Epidemiologists have used these criteria to rigorously evaluate data, and the International Programme on Chemical Safety (IPCS) has recommended their use as a means to identify causality (Sonich- Mullin *et al.*, 2001). This

rigorous process is fundamental to the decision as to whether or not a mode of action has been identified.

If there is sufficient evidence for a mode of action in animals, the next question is whether or not it is relevant to humans. To be relevant to humans, the key events that were identified in the test species should be concordant in humans. A concordance table represents this concept and analysis, where each key event is matched across species and directly to humans. If concordance is established between the test species and humans, the next question is whether or not the mode of action is still relevant to humans when considering the dose levels and kinetic differences between test animals and humans.

The collection of answers to these questions then forms the basis for a weight-of-evidence decision as to the relevance of thiamethoxam's non-genotoxic, mouse-specific hepatic tumorigenesis to human health.

A mode of action has been identified for the development of thiamethoxam-related mouse liver tumors in thiamethoxam-treated mice that includes metabolite CGA330050-induced hepatotoxicity, with exacerbation of this hepatotoxicity by metabolite CGA265307 via inhibition of inducible nitric oxide synthase, which is followed by cell death, both as necrosis and apoptosis, and increased cell replication (Green *et al.*, 2005a). These changes are proposed as the steps that lead to the tumors seen at 18 months in mice. Figure 1 is a pictorial representation of the time-related series of metabolite formation, key hepatic events, and tumor formation. The following series of three questions follows the decision logic summarized in the introduction to this paper and described by Cohen *et al.* (2004).

The often-cited "Hill criteria" (Hill, 1965) comprise a list of nine characteristics that help discriminate an *association* of events from *causation*. Whereas Hill's hallmark criteria were directed towards epidemiology, their rigorous nature can be applied as well to the discrimination of cause and effect in molecular toxicology. Faced with well-conducted and reliable data, Hill states… "Our observations reveal an association between two variables, perfectly clear-cut and beyond what we would care to attribute to the play of chance. What aspects of that Downloaded from toxsci.oxfordjournals.org by guest on February 2, 2011 - 7 - association should we especially consider before deciding that the most likely interpretation of it is causation?" (Hill, 1965) or the purpose of analyzing the causal relationship of the data that support the key events in the postulated mode of action for mouse liver tumors, the Hill criteria have been organized into groupings as follows: Strength**,** Consistency**,** and Specificity: in this analysis, obvious and well-defined effects indicate strength, consistency by repetitive correlation, and specificity by the key events that are intimately related to particular outcomes.

In a 50-week mouse study with thiamethoxam, which was designed to examine the progression of hepatic effects, the earliest change, within one week, was a marked reduction (by up to 40%) in plasma cholesterol. This was followed 10 weeks later by evidence of liver toxicity, including increased single-cell necrosis and increased apoptosis. After 20 weeks there was a significant increase in hepatic cell replication rates. All of these changes persisted from the time they were first observed until the end of the study at 50 weeks. This progression of events was consistently seen in several studies of 10, 20, or 50 weeks duration, with the hallmark indicator being a substantial decrease in plasma cholesterol levels (Green *et al.*, 2005a).

Likewise, obvious differences in metabolism between rats and mice suggest a reason why liver tumors were only seen in mice. Three key metabolites were identified and systematically evaluated for toxicological contribution to the sequence of hepatic effects. Downloaded from toxsci.oxfordjournals.org by guest on February 2, 2011 - 8 - Mice and rats both produce CGA322704 as a major blood metabolite, which suggests that this particular metabolite is not an indicatorof a species difference. However, CGA322704 does not cause liver tumors in mice (Federal Register, 2003) nor does it cause any of the hepatic changes seen with thiamethoxam and is thus considered not to be a part of causative chain of hepatic events. CGA265307 and CGA330050, on the other hand, are produced in substantially greater quantity by mice than by rats (up to 140-fold and 15-fold greater, respectively), suggesting that the metabolic pathway through CGA330050 is critical to the mode of action. In studies where these metabolites were fed to mice for at least ten weeks, CGA330050 was found to induce the same hepatic effects, and to the same degree, as thiamethoxam; however, CGA265307 alone induced none of the clinical or histopathological changes seen in the thiamethoxam-treated mice.

The role of CGA265307 was established by comparing its structural similarity to known inhibitors of inducible nitric oxide synthase (iNOS), by verifying the ability of CGA265307 to inhibit iNOS *in vitro*, and by assessing the ability of CGA265307 to exacerbate the iNOSdependent hepatic toxicity of carbon tetrachloride *in vivo*. Based on structure-activity relationships and *in vitro* and *in vivo* experimentation, CGA265307's role is thought to enhance the relatively mild hepatotoxicity induced by CGA330050, which leads to an increase in cellular death (via necrosis and apoptosis).

Differences in metabolism between mice and rats, the contributory role of specific metabolites, and the time-dependent progression of hepatic lesions were consistently seen in a series of separate studies, including two strains of mice. Furthermore, the changes noted in Downloaded from toxsci.oxfordjournals.org by guest on February 2, 2011 - 9 - the mouse are not trivial, but are significant and sustained. Taken together, these studies strongly support the postulated mode of action. Temporality and Dose-Response: Studies of 10, 20, and 50 weeks clearly delineated the time- and dose-related progression of hepatic lesions that includes early changes in indices of liver "dysfunction", most notably decreases in cholesterol, followed (at 10 weeks) with a persistently increased incidence of cellular death (single cell necrosis and apoptosis), and sustained increase in cell replication rates when measured at the 20- to 50-week time points. An increased incidence of thiamethoxam-related tumors are then noted late in the 18-month mouse study, predominantly in animals killed at the end of treatment.

These studies depict a slowly evolving, time-dependent hepatotoxicity that ultimately results in cellular attrition and replacement. Most notably, this chain of time-dependent effects occurs in a dose-response relationship that parallels the dose-related, late-life occurrence of tumors in mouse livers (Green *et al*., 2005a), giving a no-effect level of 200 ppm in the mouse for tumor incidence as well as the hepatotoxic precursor key events. Therefore, the postulated mode of action fulfills the Hill criteria with regard to temporality and doseresponse.

Plausibility**,** Coherence**,** Experiment**,** and Analogy: Taken together, these criteria speak about the believable nature of the postulated mode of action. As stated by Hill, "…the causeand- effect interpretation of our data should not seriously conflict with the generally

known facts of the natural history and biology of the disease." (Hill, 1965). The mode of action postulated here follows the known pattern of cellular death and regeneration and is consistent with published examples of chemicals that generate a similar pattern (Goldsworthy *et al*., Downloaded from toxsci.oxfordjournals.org by guest on February 2, 2011 - 10 - 1993; Butterworth and Eldridge, 1995). Non-genotoxic chemicals are known to promote the formation of tumors via various pathways that result in a higher rate of cell turnover, which results in clonal expansion of aberrant cells. Chloroform and phenobarbital are examples of hepatotoxic chemicals that result in cellular death and regeneration that leads to rodent liver tumors (Meek, *et al*., 2003). Thus, there is ample evidence in the literature to support a mode of action that incorporates regenerative hyperplasia as the fundamental step in tumor etiology. Thiamethoxam is distinguished by the time-dependent steps that lead to eneralized regenerative hyperplasia, particularly the formation of sufficient amounts of two key metabolites (CGA330050 and CGA265307), leading to cellular death, regeneration, and tumor formation.

Alternative modes of action, including genotoxicity, cytochrome P-450 induction, peroxisomal beta oxidation, and oxidative stress were considered experimentally and shown not to be viable (Green *et al*., 2005a). In summary, application of the "Hill criteria" to the postulated mode of action provides sufficient support to conclude that there is a causal relationship between the proposed "key events" in mouse liver and the formation of hepatic tumors in mice. Thus, the answer to the question "Is the Weight of Evidence Sufficient to Establish a Mode of Action in Animals?"Downloaded from toxsci.oxfordjournals.org by guest on February 2, 2011 - 11 –

Given the clearly described mode of action for thiamethoxam-related tumors in mice, which consists of a series of key events that occur in a species-, time-, dose-, and metabolitedependent fashion, the next question is whether or not this mode of action could be operative in humans. Cellular attrition and regenerative hyperplasia is a mode of action that can occur irrespective of species or, indeed, tissue. Thus, the simple conclusion is that humans could be susceptible to the thiamethoxam-related progression of key events should sufficient amounts of the relevant metabolites be generated. However, as will be described in the next section, sufficient amounts of the relevant metabolites would not be generated in humans, thereby precluding the likelihood of the key events and tumors occurring in humans. Nonetheless, this stage of the ILSI-RSI decision logic asks very simply for the qualitative possibility that the mode of action could occur in human tissue. The answer in this case is "yes," which then leads to the critical next question that addresses the realistic plausibility of such a mode of action occurring in humans.

The stage of the ILSI-RSI decision logic calls for a quantitative analysis to determine whether or not a mode of action, seen in animals, would plausibly occur in humans. Kinetic profiles and consequent species-specific responses will frame the relevance of a toxicological finding to human health. To that end, similar duration toxicity studies were conducted in rats and mice with the intention of comparing the degree of toxicological response in the rat versus the mouse and to fully characterize and quantitate the generation of critical Downloaded from toxsci.oxfordjournals.org by guest on February 2, 2011 - 12 - metabolites associated with the key events. Furthermore, *in vitro* studies were conducted in mouse, rat, and human liver preparations to compare the quantity and rate of formation of the critical metabolites (Green, 2005b).

In similar duration toxicity studies in rats and mice fed thiamethoxam for up to 50 weeks, rats did not demonstrate any of the hepatotoxic key events noted very clearly in mouse studies. The lack of these key events in rats is consistent with the lack of hepatocarcinogenicity in this species. This obvious difference between species suggests either that rats and mice respond differently to thiamethoxam and its metabolites or that rats and mice differ significantly in the generation of the key metabolites, CGA330050 and CGA265307.

In a comparative metabolism study in rats and mice fed high dietary levels of thiamethoxam (3000 and 2500 ppm respectively), plasma concentrations of CGA330050 and CGA265307 were measured at 10-week intervals over 50 weeks of continuous feeding. Two fundamental quantitative conclusions can be drawn from this study: mice generated significantly more of these two critical metabolites than rats and the generation of CGA265307 increased with time in mice but decreased in rats. After prolonged dietary administration of thiamethoxam, the plasma levels of CGA330050 and CGA265307 were 15- and 140-fold greater, respectively, in the mouse than in the rat. Given the hepatotoxicological role of these two metabolites, this *in vivo* experiment provides an explanation for the lack of response in rats and thus the difference in hepatotoxicity between rats and mice.

The question then becomes whether or not human metabolism of thiamethoxam would be more similar to rats or mice. *In vitro* comparisons of metabolic rates were conducted by using liver fractions to measure the metabolic rate constants (Km and Vmax) of Downloaded from toxsci.oxfordjournals.org by guest on February 2, 2011 - 13 - thiamethoxam's conversion to either CGA322704 or CGA330050 and the conversion of

either of these metabolites to CGA265307. Substantial differences were found that indicated a very low rate of thiamethoxam metabolism in humans. Overall, the intrinsic clearance (Vmax/Km) for the conversion of thiamethoxam to CGA265307 via CGA322704 was 371- fold lower in human liver fractions than in mouse liver and that via CGA330050 was 238- fold lower. Furthermore, human liver Km values were substantially higher (up to 21 mM) than in mice. Given that sustained high-dose feeding studies in mice generated thiamethoxam plasma levels in the range of 0.04-0.06 mM, sufficient levels of thiamethoxam could not be generated in humans to drive the metabolic pathways to any significant extent (Green *et al*., 2005b).

Indeed, rats fed for a lifetime at a rate of 3000 ppm thiamethoxam in the diet did not develop tumors and a response in humans would not be expected because metabolic rates are lower than in the rat, and exposures via diet, environment or operator use are many orders of magnitude lower than 3000 ppm.(Green *et al*., 2005b).

The concordance table recommended in the ILSI-RSI decision logic (Cohen *et al.*, 2003; Meek *et al,* 2003) is a method whereby key events can be compared across species, with the ultimate comparison to humans. The thiamethoxam shows that the initial key event is generation of the critical metabolites CGA330050 and CGA265307, with subsequent key events dependent on the formation of these key metabolites. Whereas all three species are clearly *qualitatively* capable of generating these metabolites, kinetic studies have shown that, *quantitatively*, neither rats nor humans would produce enough of these metabolites to begin the progression of hepatic key events. As a consequence, the clear conclusion can be drawn that humans would not be at risk of developing liver tumors as a result of exposure

to thiamethoxam. Downloaded from toxsci.oxfordjournals.org by guest on February 2, 2011

3.0 MATERIALS AND METHODS

3.1 The Study Area

The study was carried out in Atwima Nwabiagya district in Ashanti region.

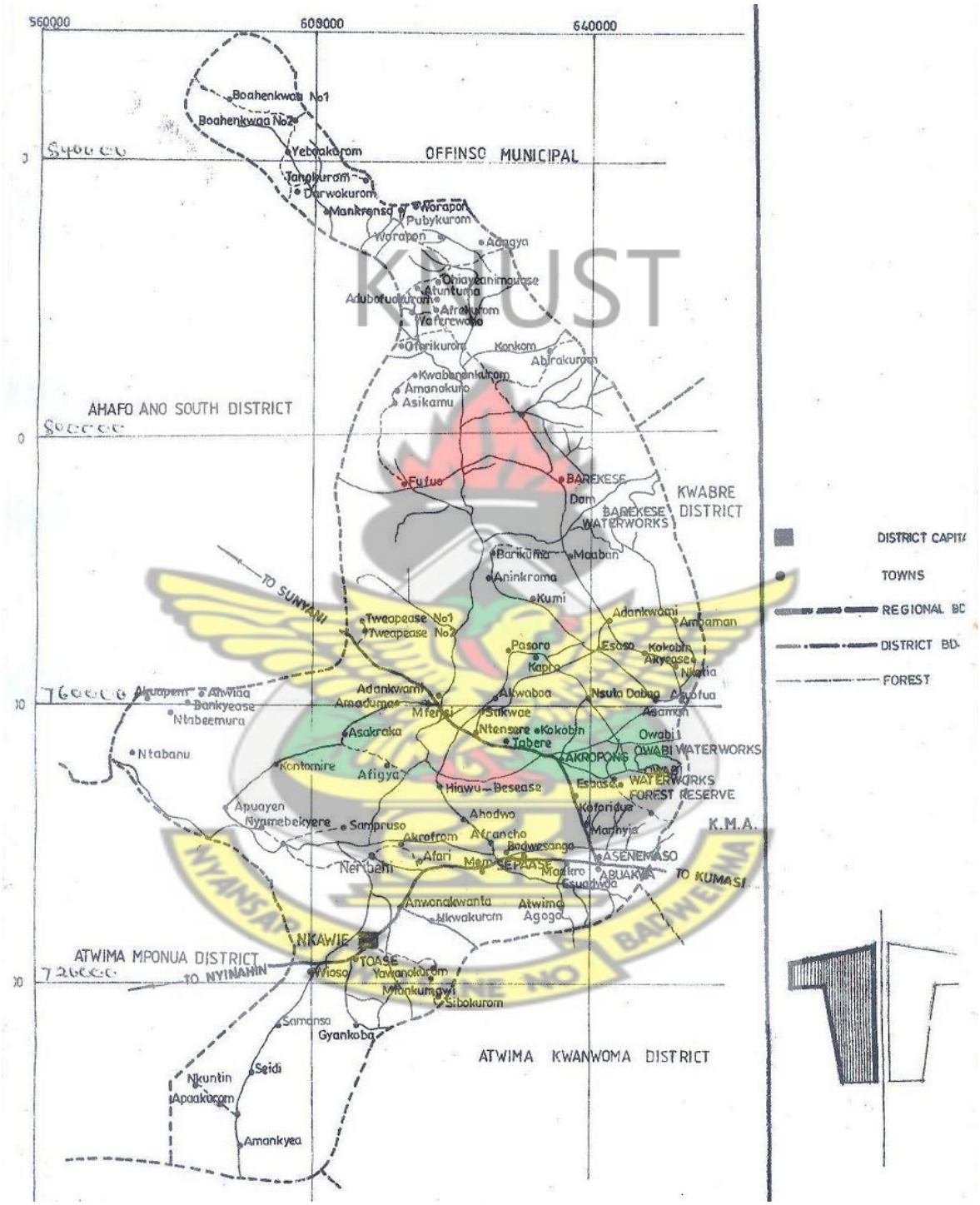


Figure 1: Map of Atwima Nwabiagya District, Showing the study areas

3.1.1 Location and Size

The district is situated in the western part of the region and shares common boundaries with Ahafo Ano South and Atwima Mponua district (to the west), Offin district (to the north), Amansie-West and Bosomtwe-Atwima kwanwoma districts (to the south), Kumasi Metropolis and Kwabre districts (to the east). The study area covers an estimated area of 294.84 sq km. The district capital (Nkawie) is situated along the Kumasi-Bibiani road and lies approximately on latitude 60 75'N and between longitude 10 45' and 20 00' west.

3.1.2 Topography and Drainage

The study area has an undulating topography. The lands have average height of about 77 metres above sea level. The high lands gentle to steep slopes. The highest points in the district can be found in the Barekese and Tabere areas.

The Offin and Owabi rivers mainly drain the surface area of the district. There are however, several streams in the district. These include Kobi and Dwahyen. Two major dams, Owabi and Barekese have been constructed across the Owabi and Offin respectively. These dams supply pipe borne water to the residents of Kumasi and its environs.

In years of above average rainfall, the Offin and the tributaries becomes flooded and overflow the banks causing damage to all crops within the confines of the floods. On the other hand in years of below average rainfall, the levels of these rivers are considerably lowered, sometimes being reduced to a series of disconnected pools. The smaller streams dry out completely in the dry seasons (February-March).

3.1.3 Climate

The district lies within the wet semi-equatorial zone marked by double maximum rainfall ranging between 170cm to 185cm per annum. The major rainfall season is from mid-March to July and minor season is between September and mid-November. Rainfall in the district is not distributed throughout the year. It is also not very reliable. It is therefore not safe to practice rain fed agriculture. Agriculture within the district must incorporate soil water conservation measures at all times to ensure good yield.

Temperature is fairly uniform ranging between 27 ^{0}C (August) and 31 ^{0}C (March).Mean relative humidity of about 87 to 91 percent is characteristic of the district. The lowest relative humidity usually occurs in February/April when they are between 83-87 in the morning and 48-67 in the afternoon.

3.1.4 Vegetation

The vegetation found in the district is predominantly the semi-deciduous type. The vegetation type has largely been disturbed by man's activities, thus, depriving it from its original valuable tree species, and other forest products. These include the Owabi Water Works Forest Reserves and Barekese Water Works Forest Reserve, which serve as water shed protection for the Offin and Owabi rivers. In addition part of the Gyemera Forest Reserve is located in the district.

Small fuel wood reserve and plantations (aforestation) have also been established to protect Owabi and Barekese water reservoirs. These plantations are composed of entirely exotic

species consisting mainly of teak, acacia, gumelina, and eucalyptus. However, through the activities of humans, parts of the forest vegetation are being lost.

3.1.5 Soil

The predominant soils in the district are the Kumasi-Asuasi/Nta-Offin compound Associations and the Bekwai-Nzema/Oda Complex Associations. The Kumasi-Asuasi Compound Associations developed over Cape Coast Granites are generally medium to coarse textured, good and structured and moderately grvelley. The soils have a fairly high moisture holding capacity. The soils are marginal for mechanical cultivation. Hand cultivation is rcommended. The soils are good for agriculture. They are suitable for tree and arable crops such as cocoa, citrus, oil palm, mangoes guava, avocado, maize, cassava, yams, cocoyams, plantain, pawpaw, groundnuts, pineapple and ginger. The valley bottom soils are good for the cultivation of rice, sugarcane and vegetable.

Soils of the Kumasi-Asuasi Compound are found at places like Nerebehi, Abuakwa, Nkawie, Toase etc. Residential activities and sand winning have currently taken most of these good agriculture lands.

The Bekwai-Nzema/Oda Complex Associations developed over Birimian phyllites, Greywacks, Schist and Gneisses are very deep, red, well drained and brown. Their moisture holding capacity is fairly high although surface layers are susceptible to dry season drought. The soils are moderately good for agriculture. The upland and slope soils

are suitable for all the tree and arable crops mentioned. The valley bottoms are good for the cultivation of rice, sugarcane and vegetables.

Soils of the Bekwai-Nzema/Oda Complex Associations are found in places like Fufuo, Mfensi, Barekese, Adankwame, Akropong, Amanchia, Bsease, Wurapong, Boahenkwa, etc.

3.1.6 Geology and Minerals

The district is underlain by the lower Birimian rocks, which consist of phyllites, greywacks, achists and gneiss, and the Cape Coast Granite. Both the lower Birimian and the Cape Coast Granite are not of the considerable economic importance since they do not bear gold and bauxite. However, the rocks (especially the lower Birimian) consist of good clay deposit. The Cape Coast Granite is a good potential for the construction industry.

3.1.7 Population

The total population of the district according to the 2000 population and housing census was (129,375) with an annual growth rate of 3%. The census revealed that the district has a sex ratio of 101:100 males to females.The projected population of the district for 2008 (using geometric methods) is 178,989 and population density 439 persons per sq km.

3.2 ADMINISTRATION OF QUESTIONNAIRE

A questionnaire was designed and administered to identify the various types of chemicals used for the control of diseases and pests of cocoa, those commonly used by farmers, frequency of use of these chemicals, kinds of protective equipment utilized and frequency

of their use; and also to gather data on health complaints of farmers. The questionnaires were pre-tested and modifications made to suit the aim and objectives of the study. The questionnaire (Appendix A) was administered to 100 individual farmers. All respondents were interviewed individually by verbally answering questions in the questionnaire.

3.3 LABORATORY EXPERIMENTS

3.3.1 Selection of chemicals

Selection of chemicals used for the laboratory experiments was based on the data obtained from the questionnaire survey.

3.3.2 Rats for experiment

The standard protocol employed in this study was based on the standard method or guidelines for health effects test in subchronic inhalation toxicity guidelines developed by USEPA (1996b) (Appendix C). Albino rats used in the study were obtained from the same supplier (the animal house of the Department of Theoretical and Applied Biology, KNUST). A total of forty-eight albino rats of sixty days old were housed and acclimated to laboratory conditions for fourteen days prior to dosing. Food and tap water were available throughout the studies ad libitum. A constant temperature of 33 $\pm$2 ^{0}C was maintained throughout the experiment (Plate 1).

After the fourteen days acclimatization, the rats were weighed and divided into four groups each. Each group was made up of six rats, representing the three main protocols of above

normal, normal, and below normal exposure concentrations of the chemicals respectively. The remaining one group, D was the control, which was exposed to only distilled water.

The dose levels were chosen on the following basis:

A. Actara (thiamethoxam)

1. Above normal 34ml stock + 16lit. of water (x2 of prescribed concentration)
2. Normal 17ml stock + 16lit, of water (prescribed concentration for the farmers)
3. Below normal 8.5ml stock + 16lit.of water (half the prescribed)

B. Akate Master (bifenthrin)

1. Above normal 60ml stock + 16lit of water (x2 of prescribed concentration)
2. Normal 30ml stock + 16lit. of water (prescribed concentration for the farmers)
3. Below Normal 15ml stock + 16lit. of water (half the prescribed)

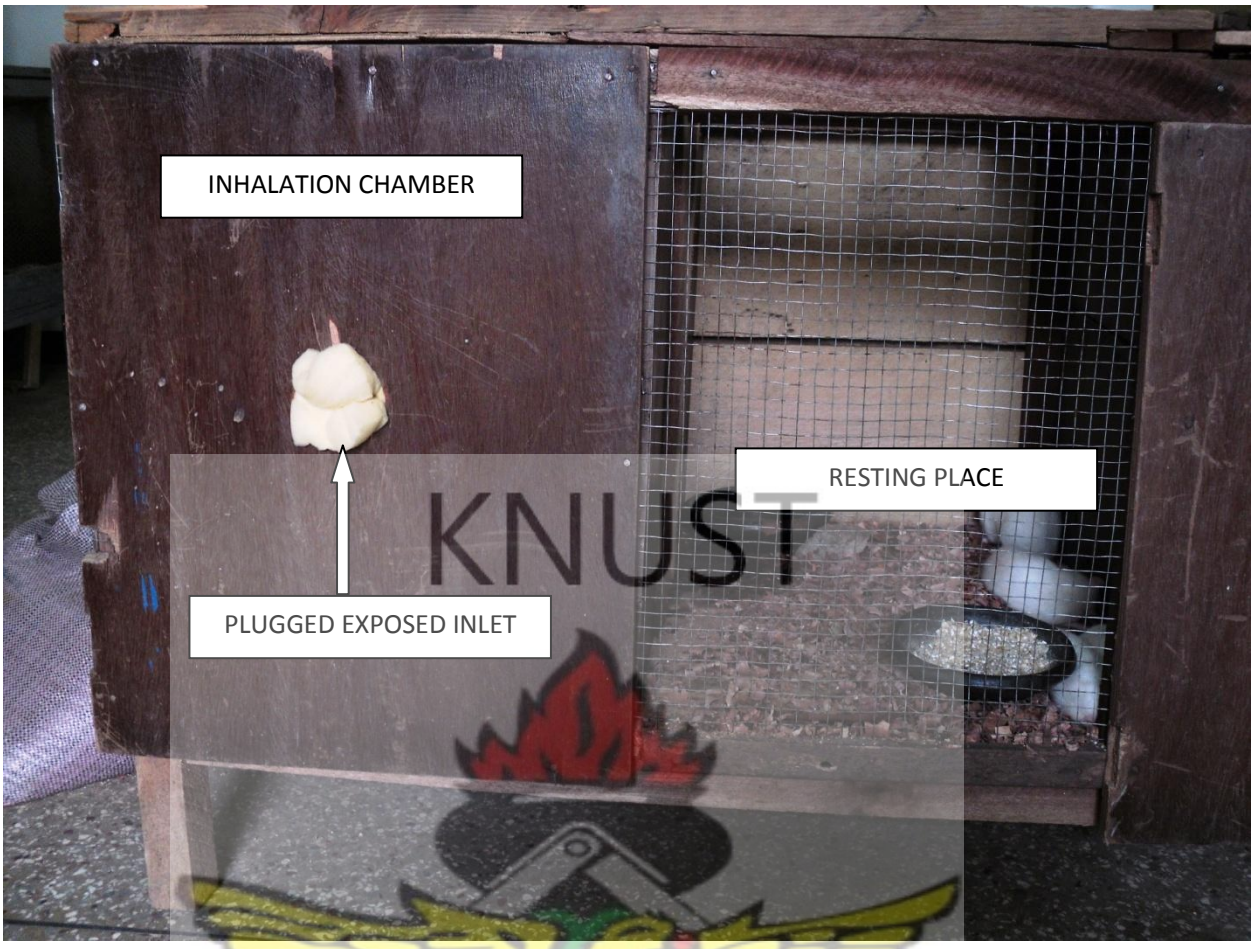


Plate 1 - Double compartment Cage with inhalation chamber and resting place

3.3.3 Evaluation of Toxicity of the Rats Exposed to Different Concentrations of chemicals

The animals were kept in a double compartment cage with inhalation chamber and resting place with dimensions of 60cm x 50cm x 48cm.

The toxicity of the rats exposed to different concentrations of the chemicals was evaluated by exposing rats to chemical aerosols generated by spraying chemical of volume 20ml/animal directly onto a target erected in the inhalation chamber (plate 2) using a spray

gun. Rats were exposed in groups of 3 for 30mins after which they were transferred to the netted resting place. In all, six rats were exposed to each concentration. As a control, the same number of rats was exposed to distilled water, as only water is mixed with the chemical for spray. Rats were weighed and examined daily for pathological changes and death. Bioactivity of the chemicals was assessed at one week exposure rest. This continued till the animals were exposed for four weeks and four weeks rest post-treatment.

After 1, 4, and 8 weeks 3 rats from each dose group, and from the control group, were sacrificed with an overdose of anaesthetics (halothane). The organs were removed and placed in formol saline. They were trimmed, embedded in paraffin wax, sectioned and stained with haematoxylin and eosin before being examined by light microscope.

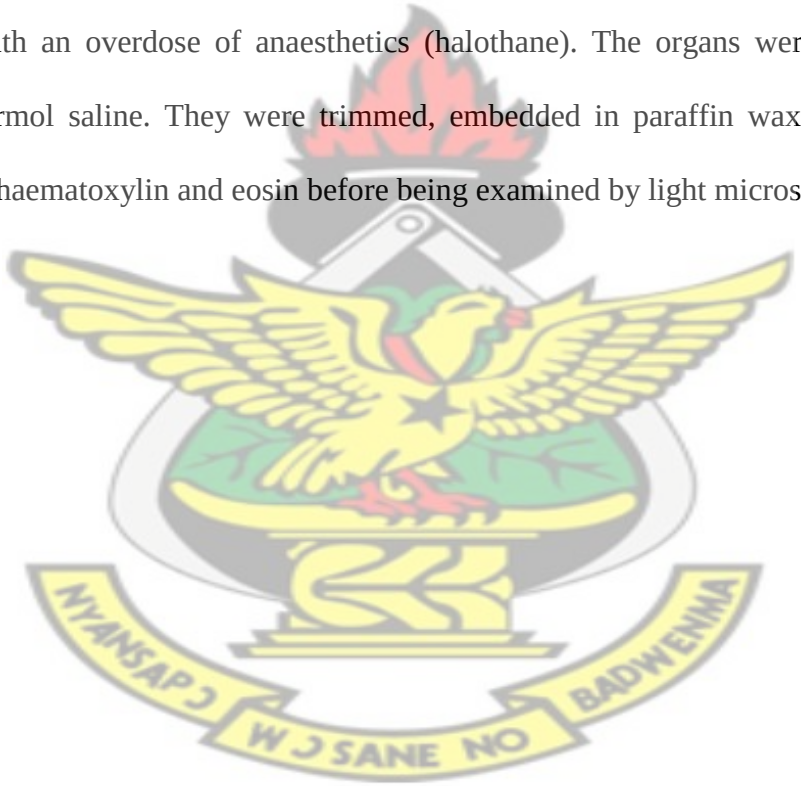


Plate 2 - EXPOSURE OF ANIMALS TO CHEMICALS

4.0 RESULTS

4.1 QUESTIONNAIRE USE

The questionnaire responses (fig. 2) revealed that almost one-third (31%) of the respondents have applied pesticides for 1 – 3 years while more than a quarter (27%) have used the pesticide for more than 10 years. 23% and 19% have applied them for 4 – 6 and 7 – 9 years respectively. Many (27%) of the gang members (government recruited members who take charge of the mass-spraying of cocoa farms) have 1 – 3 years experience while the majority (22%) of farmers have more than 9 years experience as can be seen in figure 2 below.

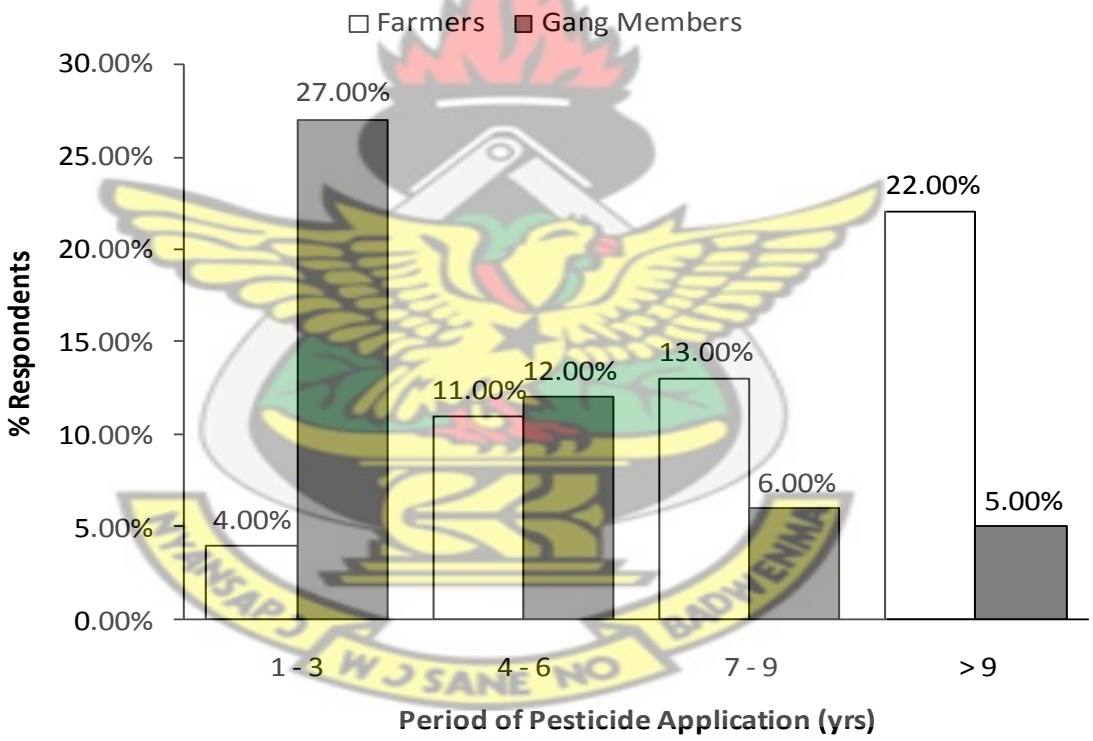


Figure 2: Working Experience of Respondents

On the type of chemicals commonly used by the farmers, approximately thirty-nine percent (39%) indicated they frequently use Akate Master (Bifenthrin) while thirty-two (32%) use Actara (Thiamethoxam) with approximately twenty-nine percent (29%) indicated they use confidor (Imidacloprid) figure 3).

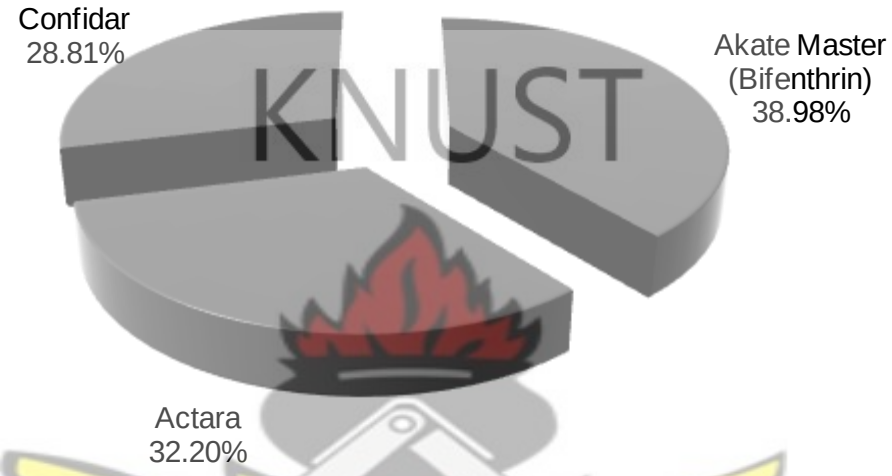


Figure 3: Chemicals commonly used by Sprayers in Nkawie District

The use of protective equipment is one of the ways for controlling workplace hazards. The results of the questionnaire survey revealed that a greater majority of the farmers in Atwima Nwabiagya district in Ashanti region wear some kind of protective clothing (figure 4). Forty-two percent (42%) of the respondents indicated they always wear protective clothing at work. About thirty-nine percent (39%) on the other hand, stated wearing at least a kind of protective but not always. Nineteen percent indicated they do not use any protective clothing at all except farm clothing.

Of the eighty-one percent of the respondents who use some kind of protective clothing or equipment, 32.10% use coverall, 14.81% also use hand glove, 12.35% prefer to use nose mask/respirators, while 29.63% use hat. In addition, 11.11% use goggles/face masks.

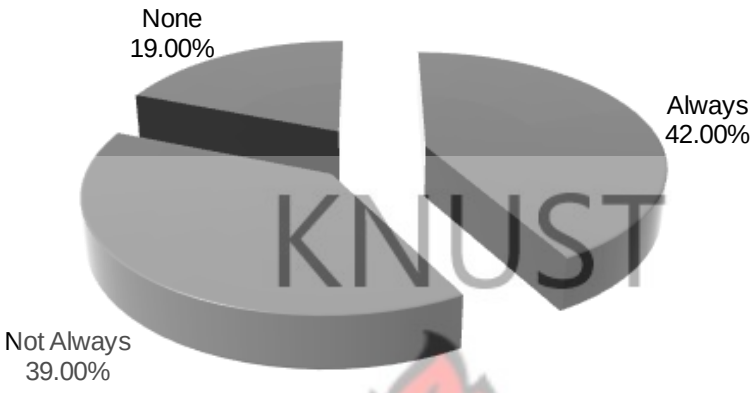


Figure 4: Use of Protective Clothing by Respondents

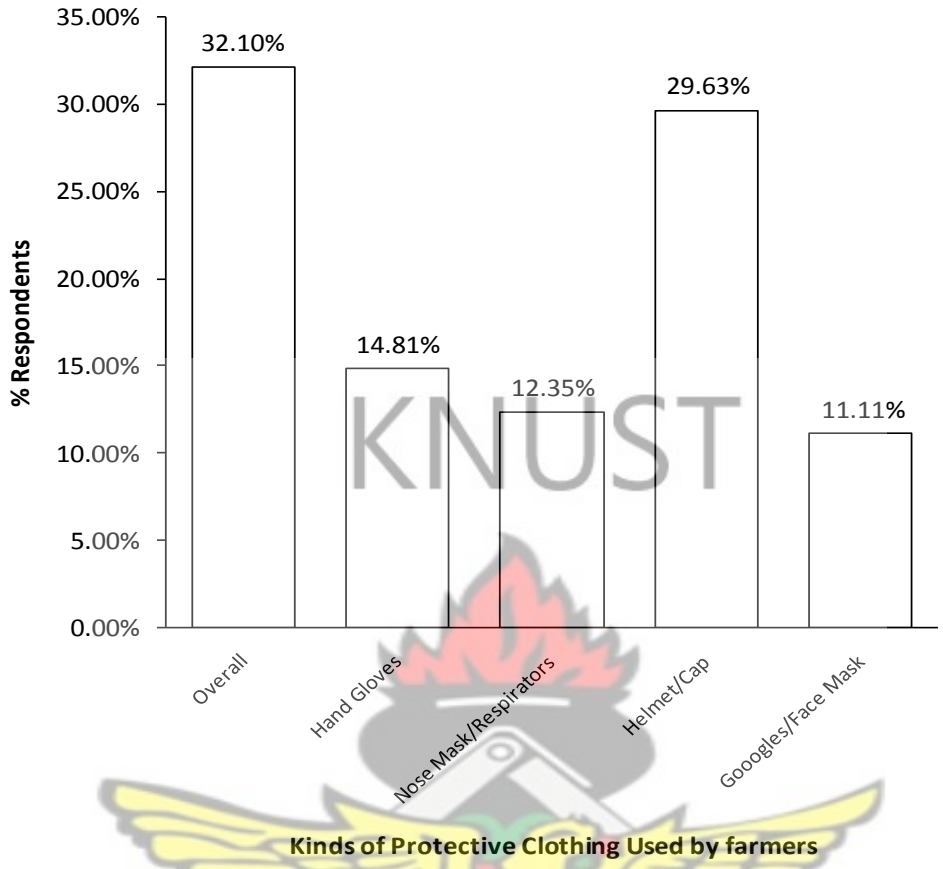


Figure 5: Kinds of Protective clothing used by respondents

Of the nineteen respondents who do not use any kind of protective clothing or equipment, 63.16% indicated they lack access to the clothing or equipment while 26.32% mentioned breathing difficulty, discomfort and the inconvenience created by some of the clothing as reasons for not using the clothing (fig. 6).

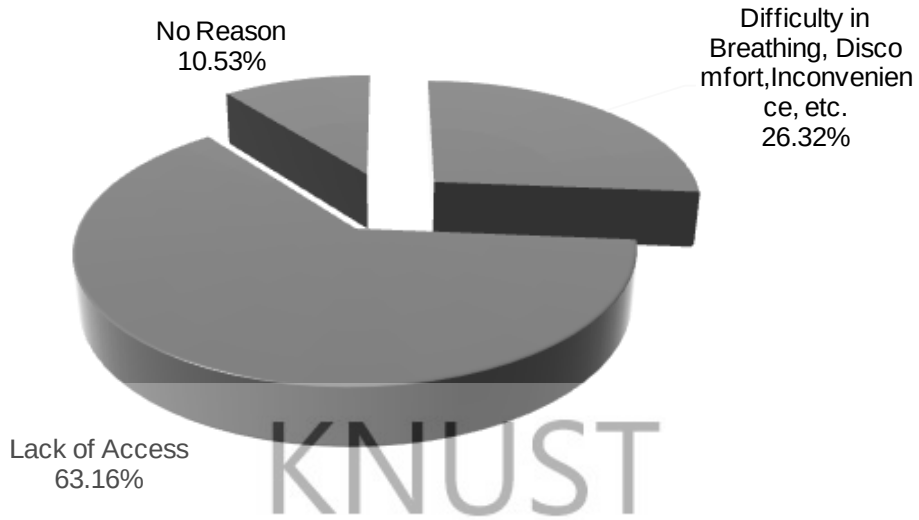


Figure 6 Reasons why some Respondents fail to wear Protective clothing

In response to whether they smoke or not, seventy-nine percent (79%) of the respondents answered in the negative (fig. 7).

Figure 7 Prevalence of Smoking in Respondents

The questionnaire survey also revealed that most of the respondents (61%) do not consume alcohol (fig. 8).

Figure 8: Prevalence of Alcohol Consumption among Respondents

On frequency of attendance at hospitals/clinics, none of the respondents indicated visiting either a clinic or drug shop daily and forty-three percent (43%) said they rarely visit the hospital (fig. 9).

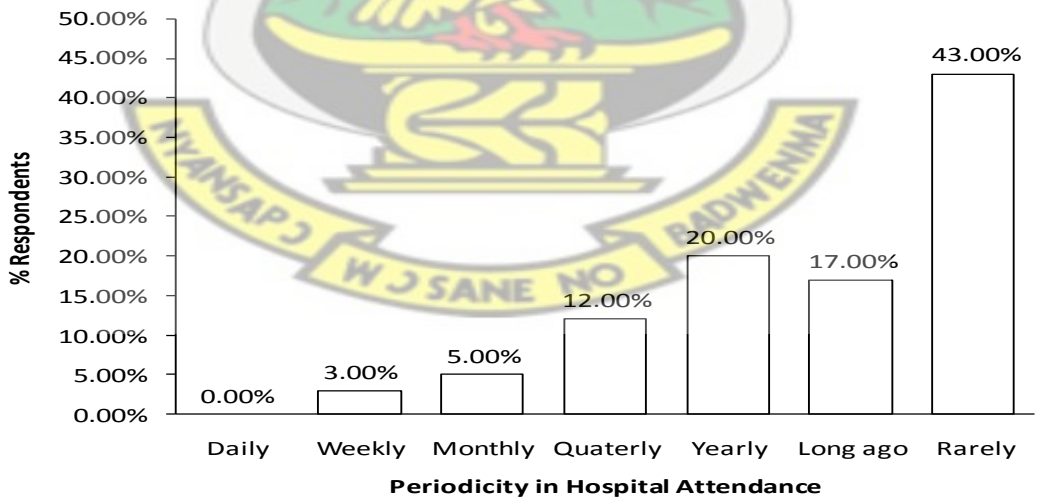


Figure 9: Frequency of Hospital Attendance by Respondents

The survey revealed that apart from the main occupation which is farming, some of the respondents also engage in other occupations. Of the twenty-nine percent (29%) who indicated engaging in other activities, sixteen percent (16%) and thirteen percent (13%) engage in driving and trading respectively (fig. 10). 71% indicated they do not engage in other activities apart from farming.

Figure 10: Other Occupations Undertaken by Respondents

On the health problems usually encountered, thirty- percent (30%) of them said they often experience headaches, followed by skin irritation (24%), Dizziness (14%), and nose irritation (fig. 11).

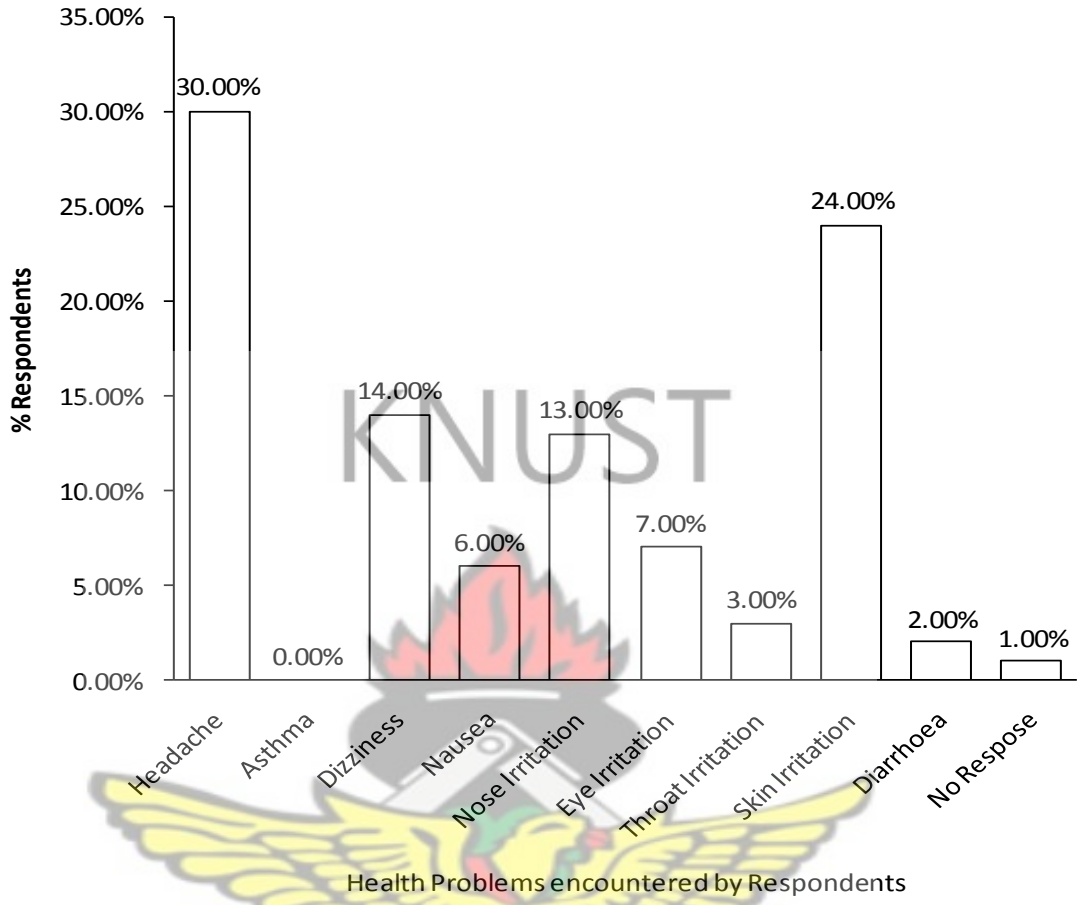


Figure 11: Health Problems usually encountered by Respondents

Respondents with long application of chemicals such as 10years said that they experienced health hazards than those with shorter period of the use. The study also revealed that moderate use of the pesticide did not significantly affect the health of the respondents ($p \geq 0.05$) fig. 12).

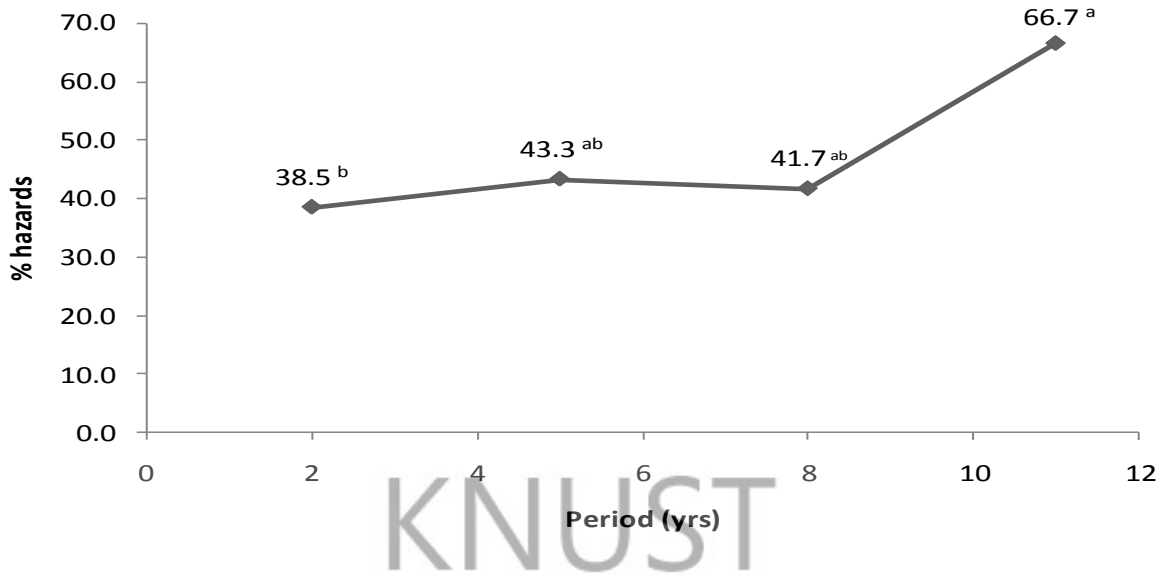


Figure 12 The Effect of Period of Pesticide Use on Health of Respondents.

The use of protective clothing led to less experience of health hazards (fig. 13), $p \leq 0.05$.a non-use cause a significantly higher incidence of health hazards (69.6%) compare to partial use (20%) and constant use (17.7%). There was no significant different from partial use and constant use.

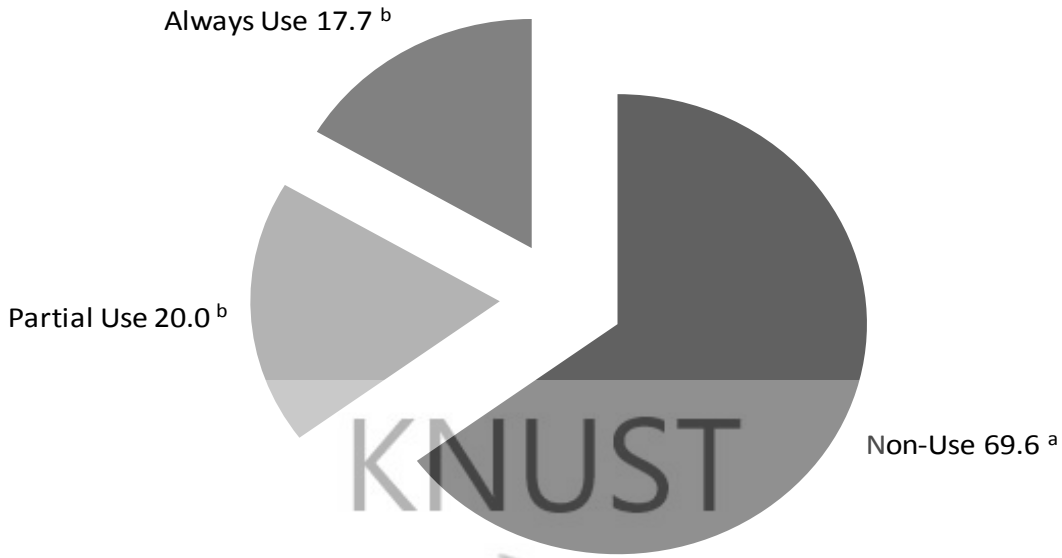


Figure 13 Effect of Use of Protective Clothing on Health of pesticide users (*a highest at p < 0.05)*

4.2 LABORATORY EXPERIMENTS

4.2.1 Evaluation of toxicity of the laboratory Rats Exposed to varying concentrations of Actara (thiamethoxam).

The results showed that the daily exposure of rats to 20ml volume of thiamethoxam at varying concentrations led to the initial signs of irritation, in coordination, tremor, salivation and irritability to sound and touch. These symptoms were subsequently followed by a period of quietness after 40minutes of exposure then sleep with recovery. These are the symptoms that often characterize exposure of the rats to poison, that is, deep sleep

followed by recovery. Rats exposed to 0.26gm/l and 0.51gm/l of thiamethoxam showed signs of tremor which lasted for over 10 minutes.

4.2.1.1 Body weights

The mean body weights of the rats exposed to high (0.51gm/l) dose was not significantly different from the medium (0.26gm/l) dose. However, these were significantly lower compare to those of the lower (0.13gm/l) dose and the no chemically exposed control (0.00gm/l) groups ($p<0.05$) as seen in figure 14.

Actara caused a dose-dependent decrease in the body weight gain of rats (Fig. 14), $p \leq 0.05$. The increase in body weight of control animals was 7.5 % and was significantly greater than body weight gain for the medium (0.26 g/l) and high (0.51 g/l) doses. In the high dose body weight actually decreased by 3.1 % and was significantly less than those of the medium and low (0.13 g/l) doses too. The low dose was not significantly different from either the medium dose or control

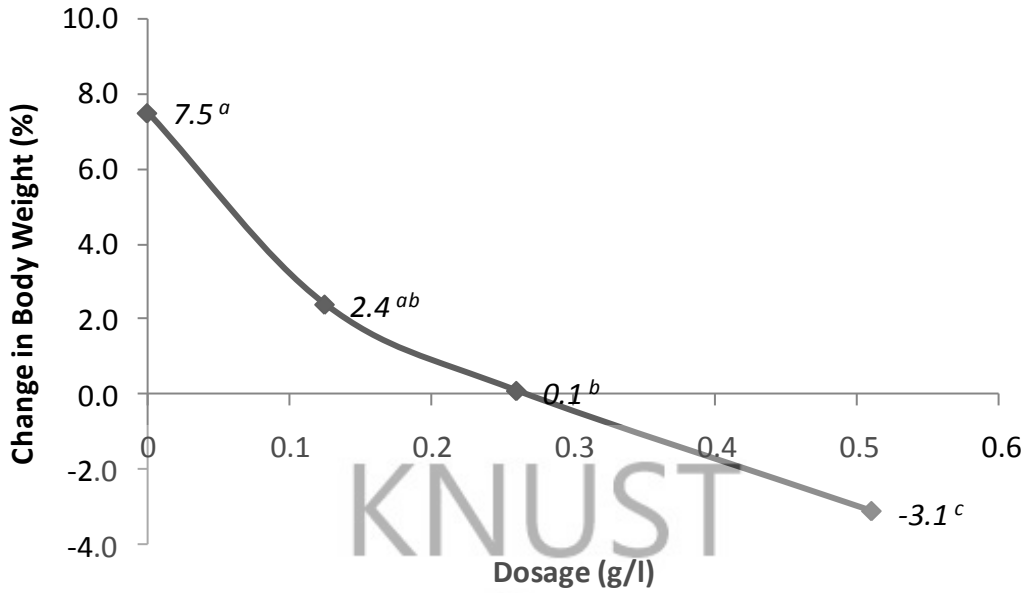


Figure 14 Change in Body Weights of Rats Exposed to Varying Concentrations of Actara

The graph shows the effect of graded doses of Actara (Thiamethoxam) on changes in the body weights of rats. *[a] significantly highest at $p \leq 0.05$*

4.2.1.2 Photomicrographs of whole organs (kidneys, liver, heart, lungs) exposed to various concentrations of Actra (thiamethoxam) including control for eight weeks duration.

a1  Actara Kidney Control - 0 gm/l (x7)	a4  Actara Kidney High - 0.51 gm/l (x7)
a2  Actara Kidney Low - 0.13 gm/l (x7)	a3  Actara Kidney Medium - 0.26 gm/l (x7)

Plate 3 -Photographs a1, a2, a3 and a4 illustrate the kidneys of a control rat (a1) and rats treated with various doses of Actara (Thiamethoxam).

There are no clear distinctions between the control and Actara-treated kidneys.

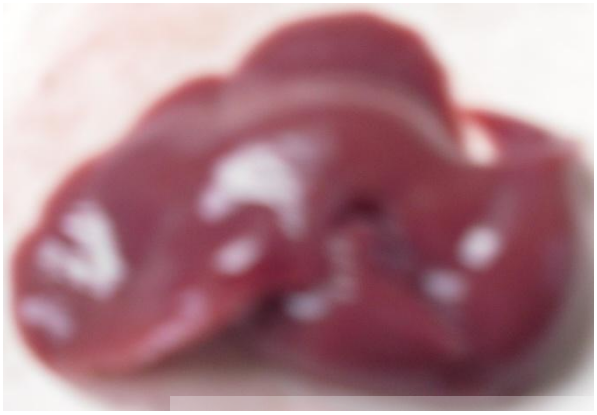
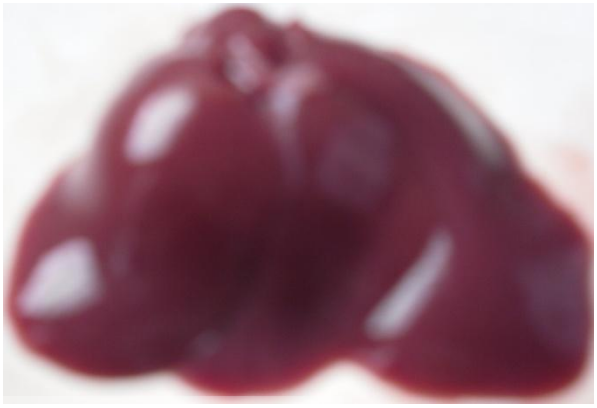
b1  Actara Liver Control - 0 gm/l (x7)	b4  Actara Liver High - 0.51 gm/l (x7)
Plate b1: A freshly looking lung of rat exposed to clean water (control) for 8 weeks.	Plate b4; A normal looking liver of rat exposed to to 0.51 gm/l concentration of Actara (thiamethoxam) for 8 weeks.
b2  Actara Liver Low - 0.13 gm/l (x7)	b3  Actara Liver Medium - 0.26 gm/l (x7)

Plate 4 -Photographs b1, b2, b3 and b4 illustrate the livers of a control rat (b1) and rats treated with various doses of Actara (Thiamethoxam).

There are no clear distinctions between the control and Actara-treated livers.

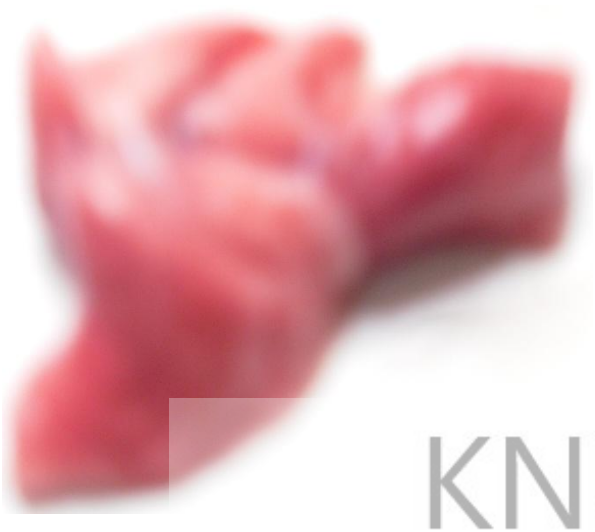
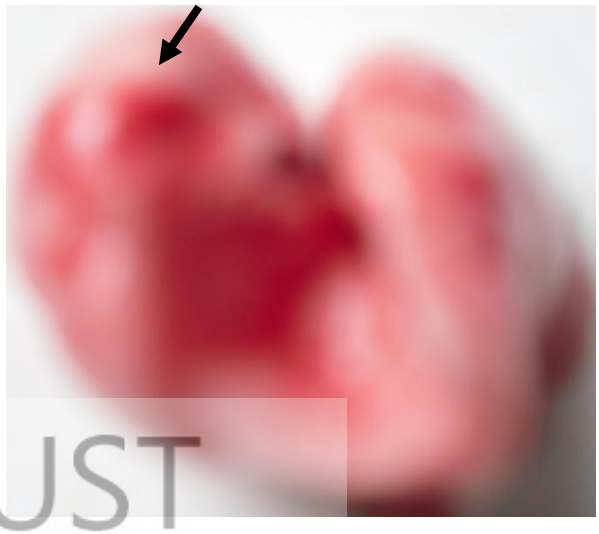
c1  Actara Lung Control - 0 gm/l (x7)	c4  Actara Lung High - 0.51 gm/l (x7)
Plate C1: Unaffected lungs of rat (control) after 8 weeks of exposure to clean water.	Plate C4 slightly inflamed lung with haemorrhage (arrowed) in rat exposed to 0.51gm/l concentration of Actara
c2  Actara Lung Low - 0.13 gm/l (x7)	c3  Actara Lung Medium - 0.26 gm/l (x7)

Plate 5 -Photographs c1, c2, c3 and c4 above illustrate the lungs of a control rat (c1) and rats treated with various doses of Actara (Thiamethoxam).

There are no clear distinctions between the control and other Actara-treated lungs, with the exception of rats treated with high (0.51gm/l) concentration which shows slightly inflamed lung (plate C4).

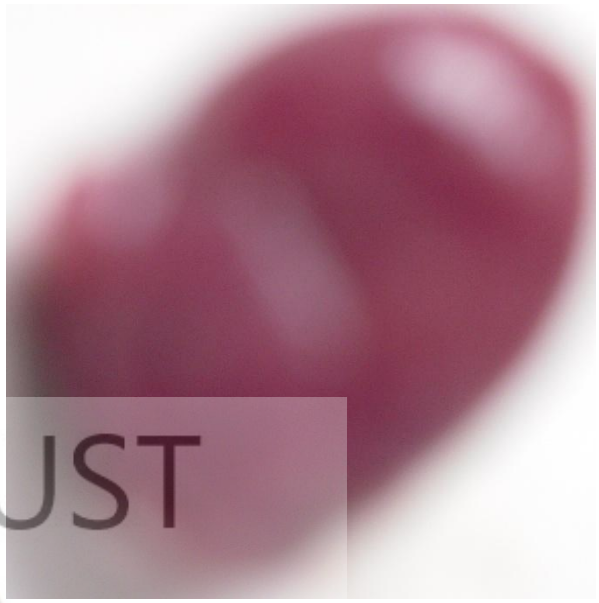
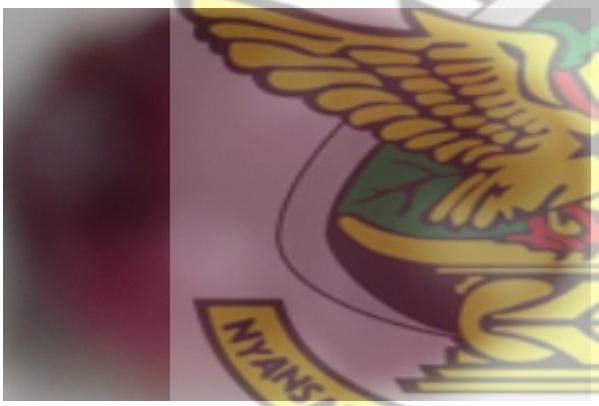
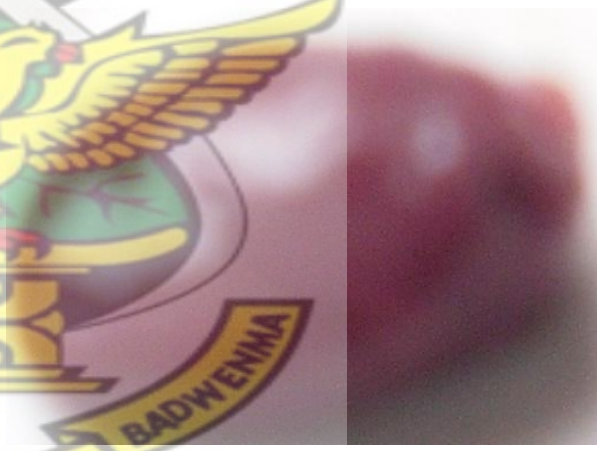
d1  Actara Heart Control - 0 gm/l (x7)	d4  Actara Heart High - 0.51 gm/l (x7)
d2  Actara Heart Low - 0.13 gm/l (x7)	d3  Actara Heart Medium - 0.26 gm/l (x7)

Plate 6 -Photographs d1, d2, d3 and d4 illustrate the Hearts of a control rat (d1) and rats treated with various doses of Actara (Thiamethoxam).

There are no clear distinctions between the control and Actara-treated Hearts.

4.2.1.3 Histopathology

The organs of the rats (liver, lung, kidney, heart) sample were removed and weighed. The organ samples were processed for paraffin embedding and mounted in paraffin block (containing the tissues of the organs removed). Serial sections were prepared from paraffin blocks, stained with haematoxylin & eosin, and examined under using microscope.

Mortality was not affected by the treatment. Histopathology examinations of the organs did not find a clear treatment related effect in rats exposed to the varying concentrations of Actara in 8 weeks exposure as Green et al 2005 observed. However, there were signs of tumour development and reduction of lung size in two rats after the 8 weeks exposure to 0.51gm/l of thiamethoxam. Some signs observed included changes in lung colour, from bright to dull as well as haemorrage (plate c4) after the duration of the exposure, lungs of rats exposed to 0.26gm/l and 0.13gm/l as well as the control showed no signs of toxicity (plate c1, c2 and c3.).

The enlargement of alveoli sac which led to fluid filling air spaces of the lungs were observed in three rats exposed to high (0.051gm/l) concentration of thiamethoxam for 8weeks. This symptom typically characterises partial pulmonary oedema. However, apart from the partial oedema and tumour signs observed after 8 weeks on the lungs of two rats in the 0.5mg/l concentration, no signs of toxicity observed on the rest of the organs in all the treatment groups.

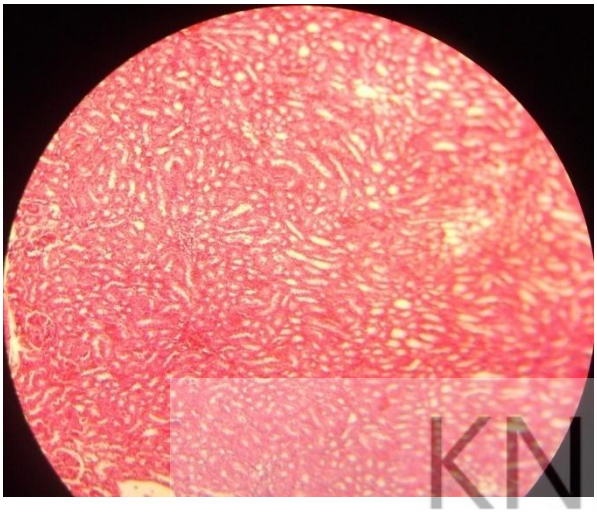
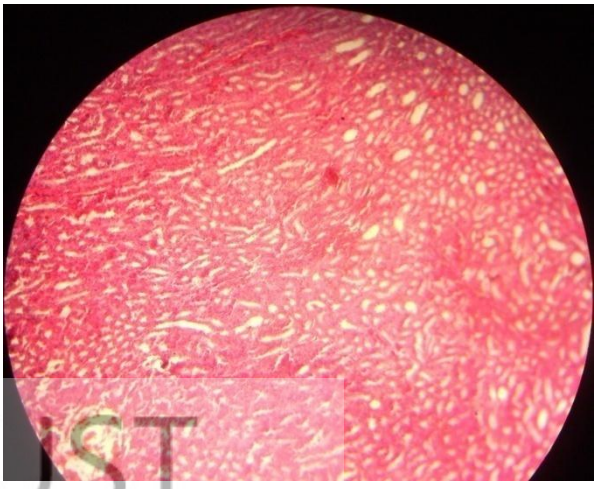
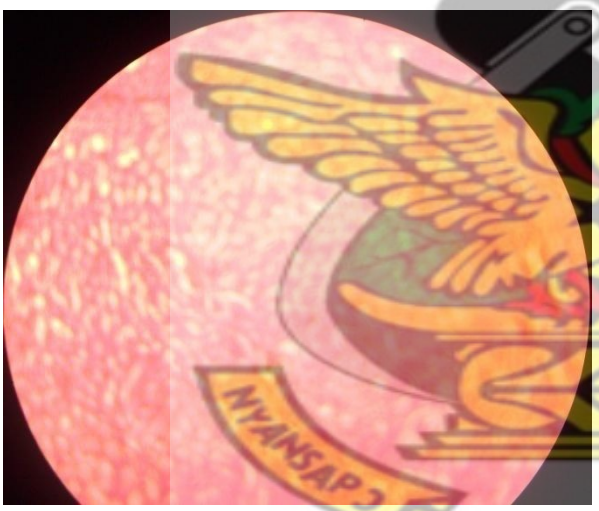
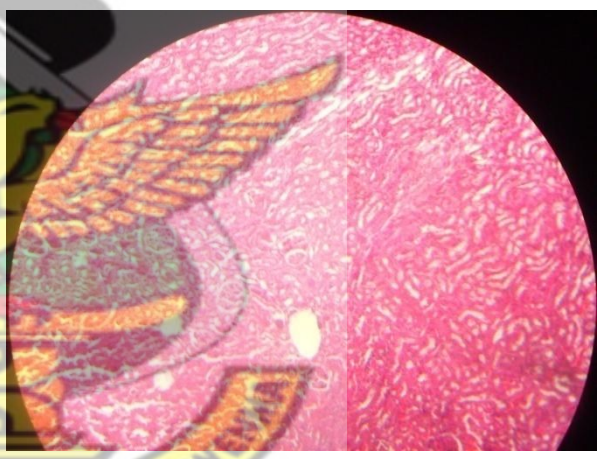
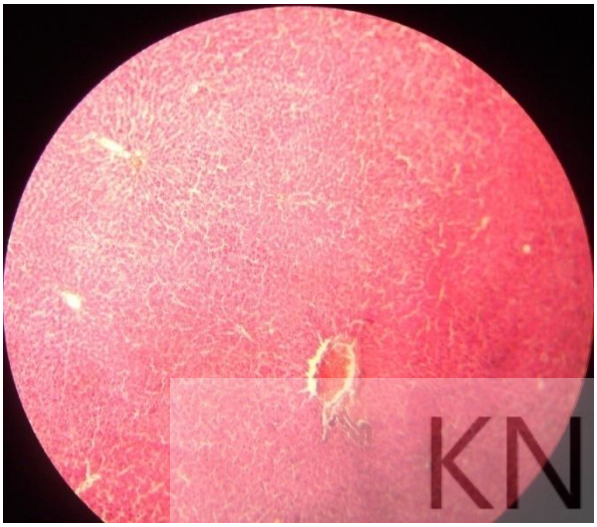
a1  Actara Kidney Control - 0 gm/l (x10)	a4  Actara Kidney High - 0.51 gm/l (X10)
a2  Actara Kidney Low - 0.13 gm/l (X10)	a3  Actara Kidney Medium - 0.26 gm/l (X10)

Plate 7 -Photomicrographs a1, a2, a3, a4 illustrate the kidneys of a control rat (a1) and rats treated with Actara (Thiamethoxam x10).

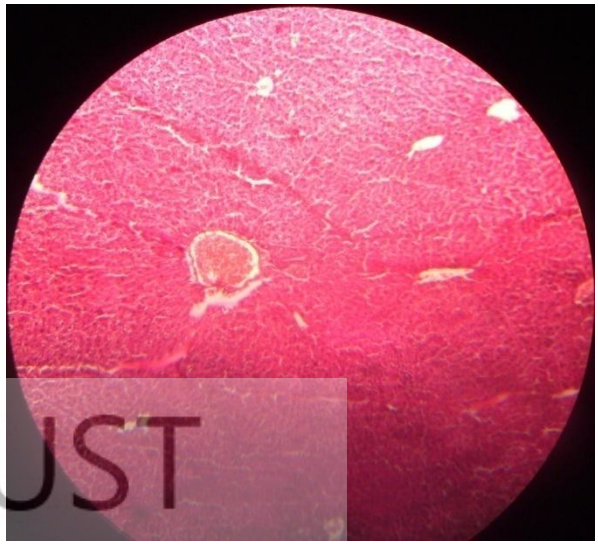
There are no clear distinctions between the control and Actara-treated kidneys.

b1



Actara Liver Control - 0 gm/l (X10)

b4

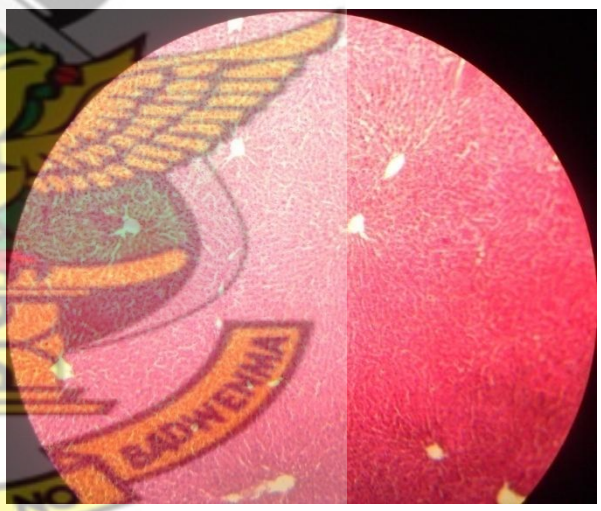


Actara Liver High - 0.51 gm/l (X10)

b2

Actara Liver Low - 0.13 gm/l (X10)

b3

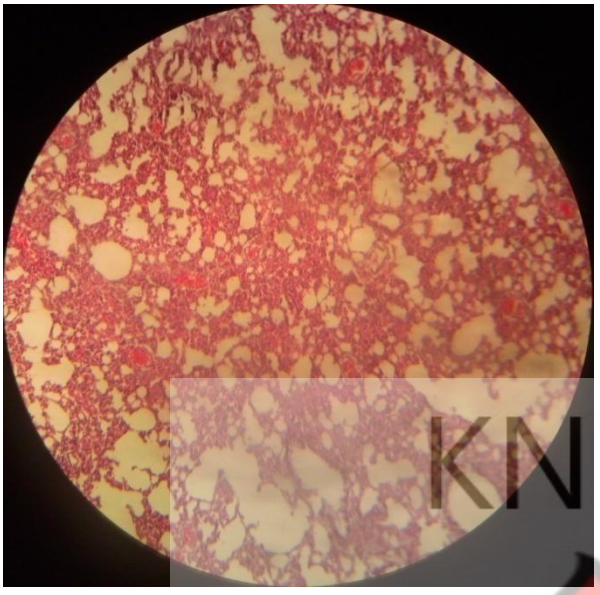


Actara Liver Medium - 0.26 gm/l (X10)

Plate 8 -Photomicrographs b1, b2, b3 and b4 illustrate the livers of a control rat (b1) and rats treated with various doses of Actara (Thiamethoxam).

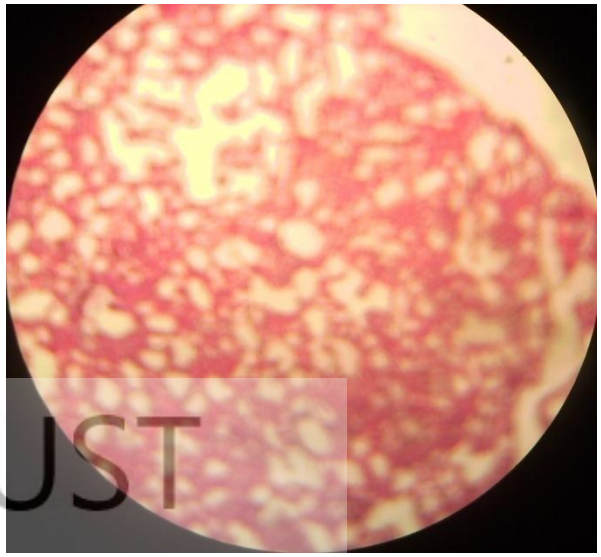
There are no clear distinctions between the control and Actara-treated livers.

c1



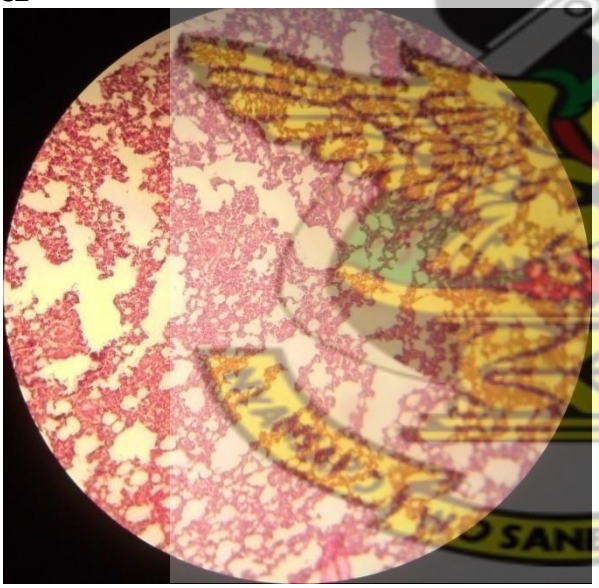
Actara Lung Control - 0 gm/l (X10)

c4



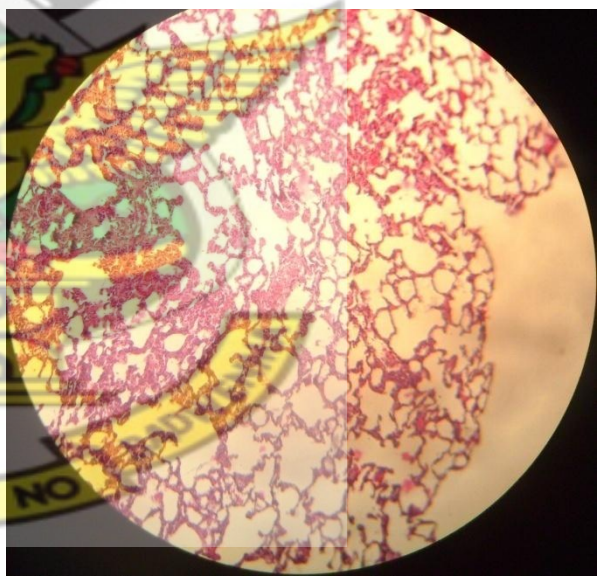
Actara Lung High - 0.51 gm/l (X10)

c2



Actara Lung Low - 0.13 gm/l (X10)

c3



Actara Lung Medium - 0.26 gm/l (X10)

Plate 9 -Photomicrographs c1, c2, c3 and c4 are the lungs of a control rat (c1) and rats treated with various doses of Actara (Thiamethoxam).

There were no clear distinctions between the control and Actara-treated lungs.

4.2.2 Evaluation of Toxicity of the Rats Exposed to Different Concentrations of Akate Master (Bifenthrin).

Exposure through inhalation for 8 weeks did not show any death or any pathological finding, but irritation and bifenthrin intoxication were observed. These effects were not much at 0.26mg and 0.5mg doses which generally persisted, but did not worsen, with continued treatment beyond 4 weeks of exposure.

4.2.2.1 Body Weights

Weight loss was significantly observed at $p < 0.05$ (fig. 12) between doses of 0.1gm/l and 0.05gm/l.The high (0.1gm/l) and medium (0.05gm/l) doses were consistently lower than the low (0.025gm/l) and the no chemically exposed control group (0.00gm/l).

The chemical (Akate Master) caused a significant reduction in body weight gain (figure 12)

$P \leq 0.05$. All the doses low (0.025gm/l), medium (0.05gm/l) and high (0.1gm/l) caused a significant reduction in body weight gain.

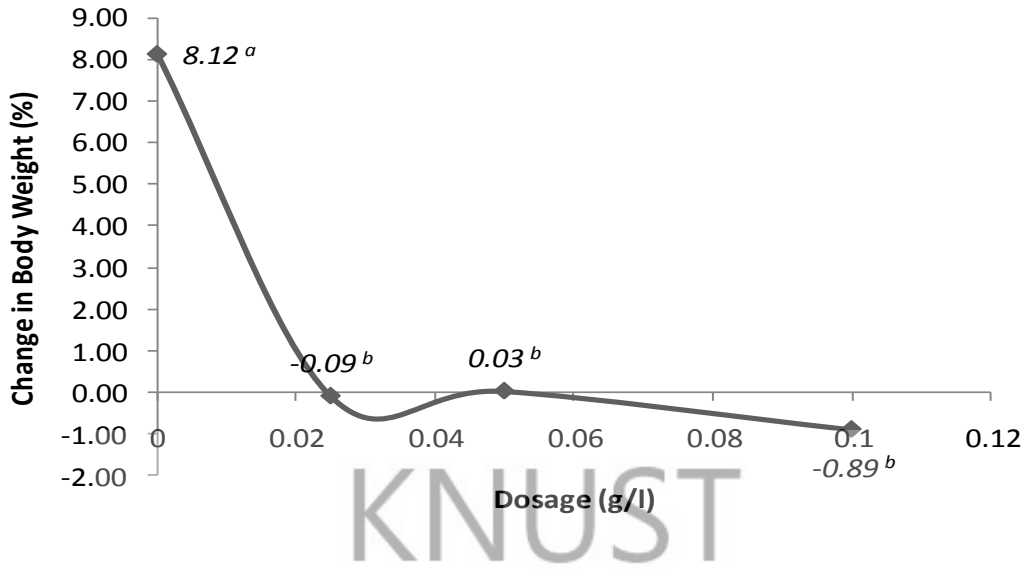


Figure 15. Change in Body Weights of Rats Exposed to Varying Concentrations of Akate Master

The graph shows the effect of graded doses of Akate Maste (Bifenthrin) on changes in the body weights of rats. [a] *Significantly highest at $p \leq 0.05$*

4.2.2.2 Photomicrographs of whole organs (kidneys, liver, heart, lungs) exposed to various concentrations of Akate Maste (Bifenthrin) including control for eight weeks duration.

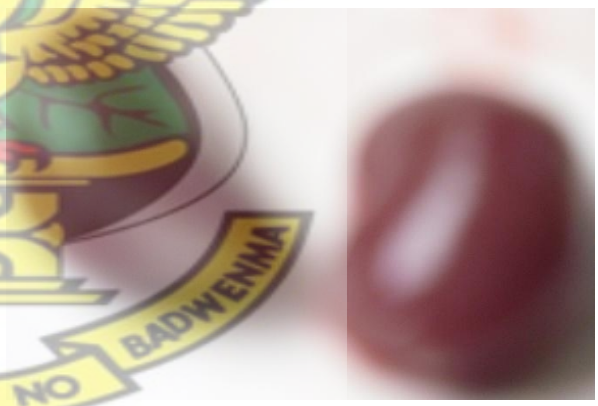
<table>
<tr><td>e1
 
Akate Master Kidney Control - 0 gm/l (x7)</td><td>e4
 
Akate Master Kidney High - 0.1 gm/l (x7)</td></tr>
<tr><td>e2
 
Akate Master Kidney Low - 0.025 gm/l (x7)</td><td>e3
 
Akate Master Kidney Medium - 0.05 gm/l (x7)</td></tr>
</table>

Plate 10 -Photographs e1, e2, e3 and e4 illustrate the kidneys of a control rat (e1) and rats treated with various doses of Akate Master (Bifenthrin).

There are no clear distinctions between the control and Akate Master-treated kidneys.

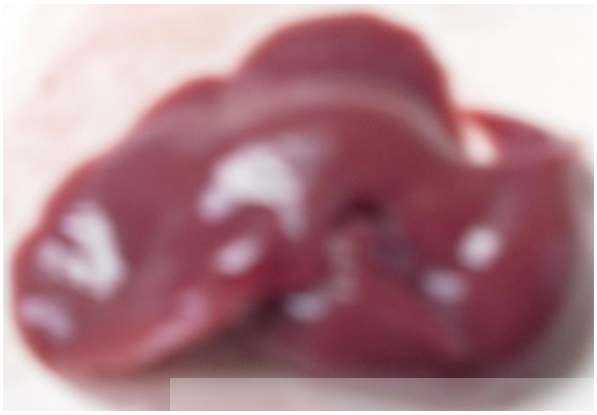
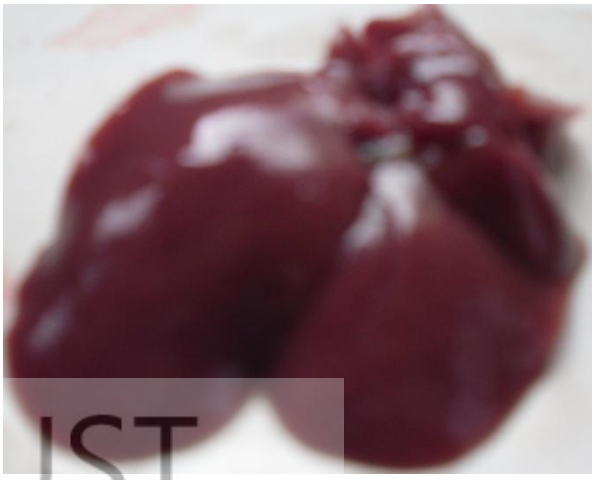
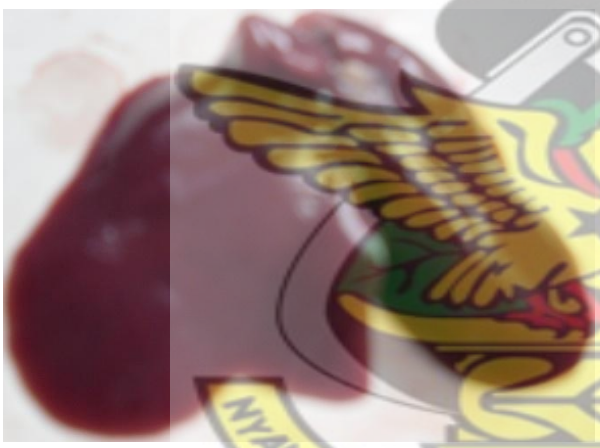
f1  Akate Master Liver Control - 0 gm/l (x7)	f4  Akate Master Liver High - 0.1 gm/l (x7)
f2  Akate Master Liver Low - 0.025 gm/l (x7)	f3  Akate Master Liver Medium - 0.05 gm/l (x7)

Plate 11 - Photographs f1, f2, f3 and f4 illustrate the livers of a control rat (f1) and rats treated with various doses of Akate Master (Bifenthrin).

There are no clear distinctions between the control and Akate Master-treated livers.

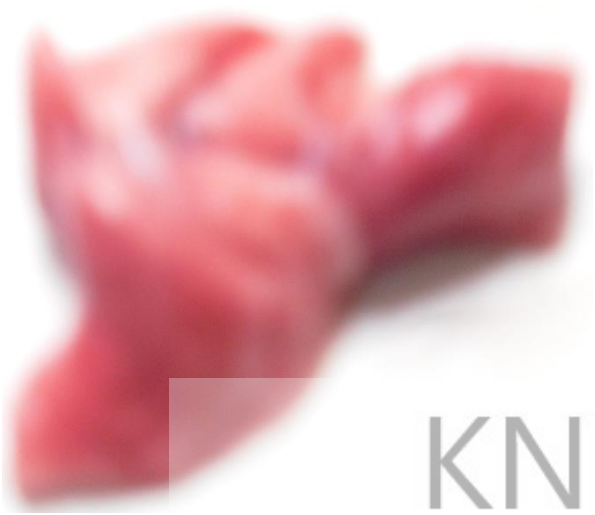
g1  Akate Master Lung Control - 0 gm/l (x7)	g4  Akate Master Lung High - 0.1 gm/l (x7)
g2  Akate Master Lung Low - 0.025 gm/l (x7))	g3  Akate Master Lung Medium - 0.05 gm/l (x7)

Plate 12 -Photographs g1, g2, g3 and g4 illustrate the lungs of a control rat (g1) and rats treated with various doses of Akate Master (Bifenthrin).

There are no clear distinctions between the control and Akate Master-treated lungs.

h1  Akate Master Heart Control - 0 gm/l (x7)	h4  Akate Master Heart High - 0.1 gm/l (x7)
h2  Akate Master Heart Low - 0.025 gm/l (x7))	h3  Akate Master Heart Medium - 0.05 gm/l (x7)

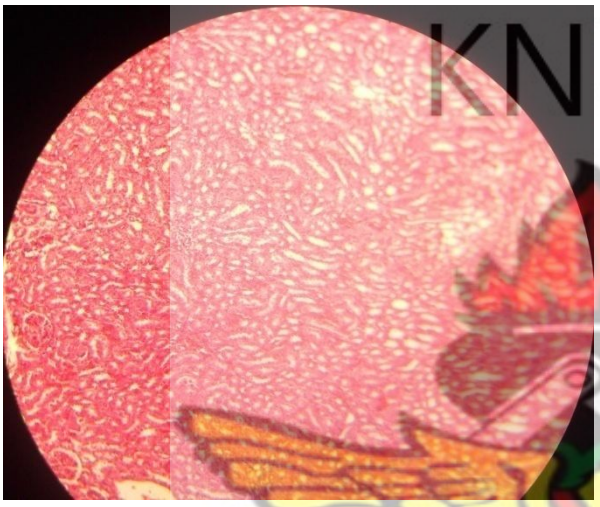
Plate 13 -Photographs h1, h2, h3 and h4 illustrate the Hearts of a control rat (h1) and rats treated with various doses of Akate Master (Bifenthrin).

There are no clear distinctions between the control and Akate Master-treated Hearts.

4.2.2.3 Histopathology

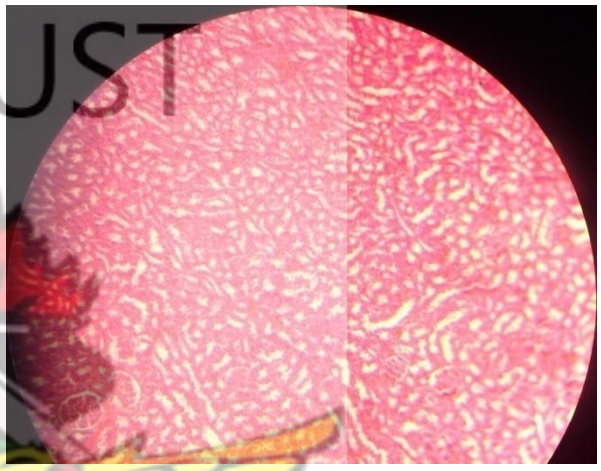
Histopathological examination did not show any evidence of a significant strain difference in response in the rats used in this study. The histopathological information is shown in plates below. This means that at highest dose (0.51g), no histopatholigical changes either in the nervous system or in other tissues or organs were observed. This confirms the finding of Wolansky M.J *et al*., 2006 that significant pathological effects are likely to be observed at dose of 0.8mg/L, air or aerosol for 4hours through nose.

d1



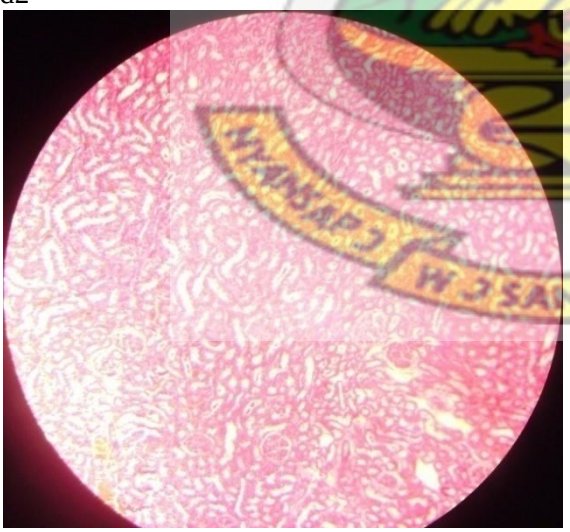
Akate Master Kidney Control - 0 gm/l (X10)

d4



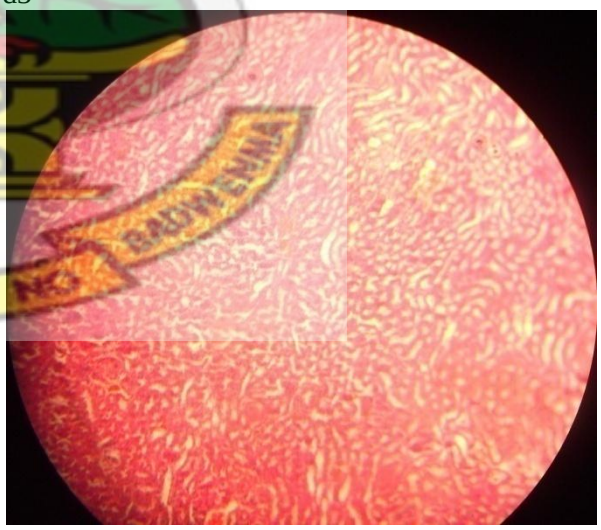
Akate Master Kidney High - 0.1 gm/l (X10)

d2



Akate Master Kidney Low - 0.025 gm/l (X10)

d3

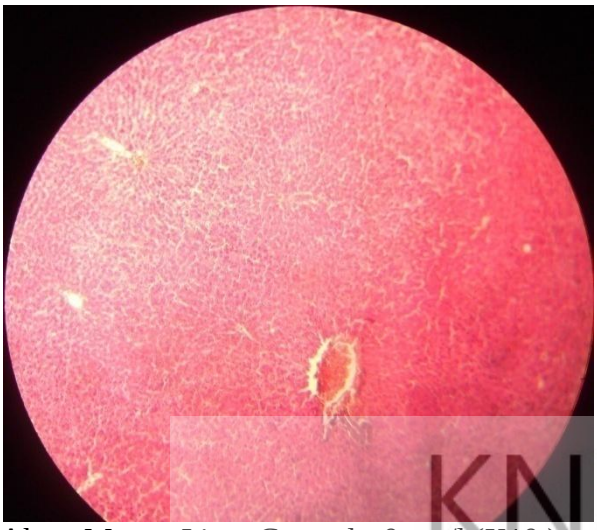


Akate Master Kidney Medium - 0.05 gm/l (X10)

Plate 14 -Photomicrographs d1, d2, d3 and d4 illustrate the kidneys of a control rat (d1) and rats treated with various doses of Akate Master (Bifenthrin).

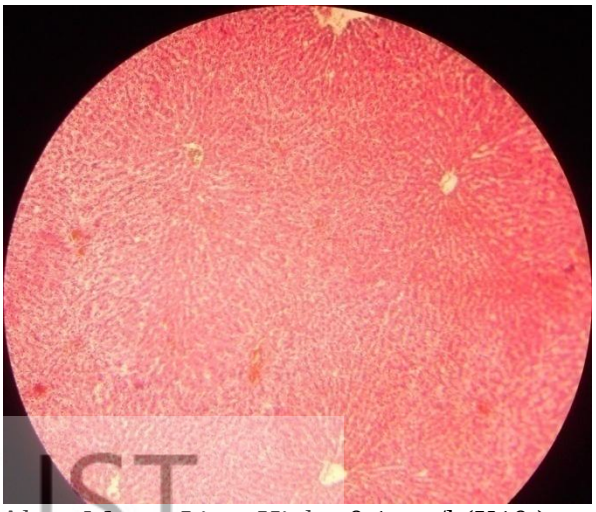
There are no clear distinctions between the control and Akate Master-treated kidneys.

e1



Akate Master Liver Control - 0 gm/l (X10)

e4



Akate Master Liver High - 0.1 gm/l (X10)

e2

Akate Master Liver Low - 0.025 gm/l (X10)

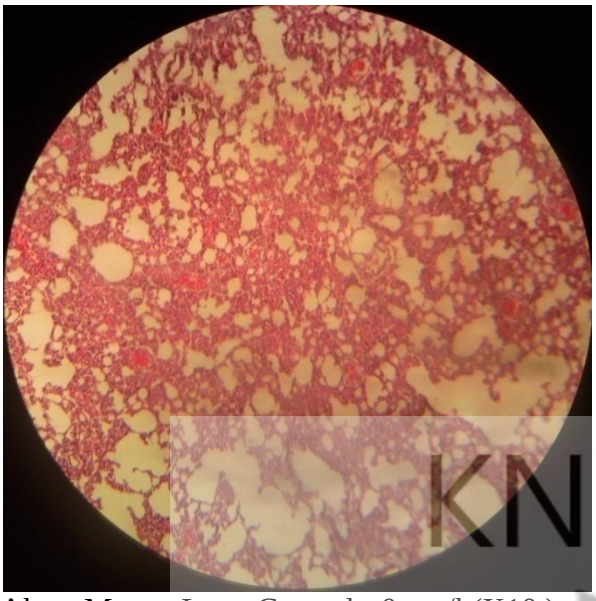
e3

Akate Master Liver Medium 0.05 gm/l (X10)

Plate 15 -Photomicrographs e1, e2, e3 and e4 illustrate the livers of a control rat (e1) and rats treated with various doses of Akate Master (Bifenthrin).

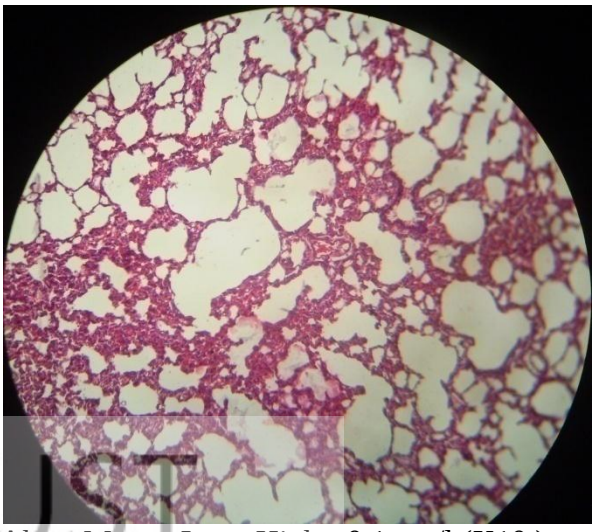
There are no clear distinctions between the control and Akate Master-treated livers.

f1



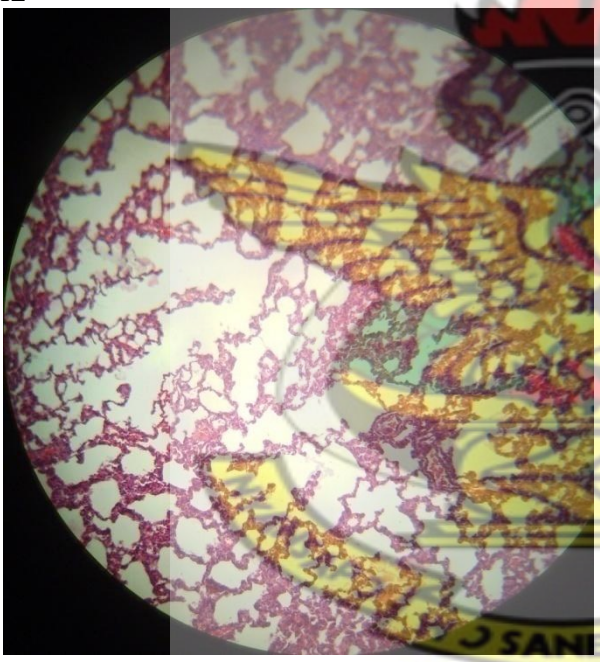
Akate Master Lung Control - 0 gm/l (X10)

f4



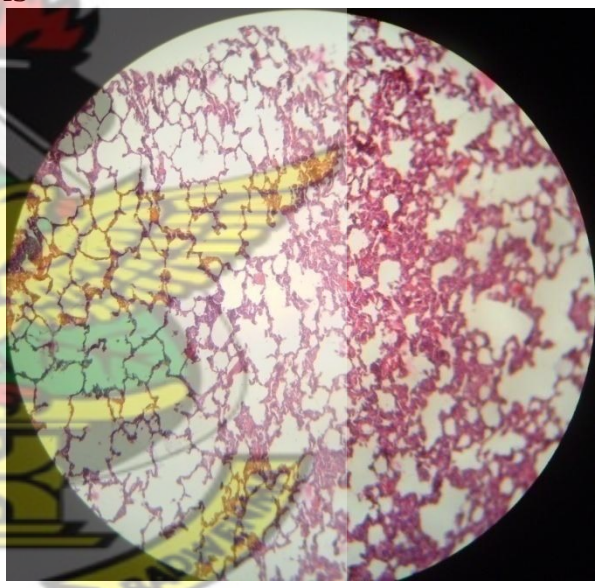
Akate Master Lung High - 0.1 gm/l (X10)

f2



Akate Master Lung Low - 0.025 gm/l (X10))

f3



Akate Master Lung Medium - 0.05 gm/l (X10)

Plate 16 -Photomicrographs f1, f2, f3 and f4 illustrate the lungs of a control rat (f1) and rats treated with various doses of Akate Master (Bifenthrin).

There are no clear distinctions between the control and Akate Master-treated lungs.

5.0 DISCUSSION

5.1 Questionnaire Administration

The results of the questionnaire data revealed that the process of mixing the chemicals for spraying cocoa by farmers produced health hazards. In testing the purity of the chemicals before mixing with water, the sprayers inhale the chemical in question directly through their nose. By inhaling such hazardous substances like bifenthrin, thiamethoxam and imidacloprid cause respiratory tract irritation with cough, mild dyspnoea, sneezing and rhinorrhea.

Another situation is in the process of spraying, the chemical mists settle on plant leaves where the spray takes place and this may be ingested by other beneficial organisms in the environment as this may cause dietary poisoning to the non-target organisms such as humans, wildlife and bees. A similar work was done by Roberts (1999), which revealed that an obvious effect of using chemicals to kill is that one is likely to kill more than just the desired organism which the present study has confirmed.

The present study also showed that 81% of the chemicals applicants wear some kind of protective clothing or equipment, only 32.10% and 12.35% of them wear complete overall and nose mask respectively (figure 5). A related study conducted by World Health Organization of Pesticides Evaluation Schemes (WHOPES, 2005) to assess worker exposure to bifenthrin during spraying of this hazardous chemical revealed that, the use of protective gloves to reduce skin contact of the solvent was not regular. This was observed at the workplace of the respondents that, protective clothing was hardly used especially

when mixing the chemicals for spraying on the cocoa farms. This could lead to skin disorder and related problems.

The questionnaire survey also indicated that Personal hygiene contribute to the level of risk to the users. Eating, improper washing and cleaning chemicals deposits and spills on hands prior to eating could lead to substance ingestion. It was observed by the present study that the sprayers pour the chemical residue after cleaning on the land without taking into consideration the other organisms that are not their target. A similar finding was reported by Waibel (1994); Gerken *et al*., (2001) that chemical residues on land find their way to waterbodies causing water pollution.

The present study further revealed that, 30% of respondents had experienced headaches, skin irritation 24%, and dizziness 14% (figure 11). This confirms the work of Browning (1965) that acute or chronic health effects often resulting from hazardous substances include respiratory tract irritation, dizziness, shortness of breath, nausea and headaches. A related study by Reed (1991) that, exposure indicated that high concentrations of thiamethoxam and bifenthrin in both short and long- term effects on the nervous system, coordination, dizziness, confusion and changes in one's sense of balance.

It must also be noted that, these signs and symptoms reported in exposed subjects might not be the result of skin reactions, but signs of peripheral nerve involvement, which is supported by He *et al*., (1988). It may be that, only paraesthesia could clearly be attributed to exposure to bifenthrin, whereas nausea, headache and dizziness might be induced organic solvents or tiredness.

The questionnaire survey further revealed that most farmers have applied the chemicals for a longer period than the mass spraying gang members (figure 2). It was observed that, it was mostly farmers who do not use the protective clothing because they have been neglected by the government. Instead, were given to the mass- spraying members. This may explain why majority farmers experience higher health hazards.

In addition my observation made in the present study, the main route of exposure in workers applying the compounds (bifenthrin and thiamethoxam) in agriculture is the skin and inhalation. A similar observation was made by IPCS, (1990), and this makes the use of protective clothing very relevant in applying the chemicals to control diseases and pests of cocoa trees. However, majority of the spraymen (63.16%) who lacked access to this important equipment were mostly farmers who do not perhaps see any importance in using the protective equipment. And this possibly explains why a ($p \leq 0.05$) higher health hazards associated with the non use of the protective clothing (figure 12). Thus a significant number of respondents who do not use protective clothing experienced some form of hazards.

None of the respondents indicated that they visit the hospital or drug shops daily while 43% said they rarely do so (figure 9). This situation may be due to the fact that most farmers are reluctant in reporting their health problems to the hospital. It may also be attributed to the fact that most of the symptoms of the chemicals last not more than 24hours, which in some cases last up to 3 days, as was reported by Zhang *et al*., 2002. Seventy-one percent (71%) have no other jobs aside farming and the rest (29%) engage in other jobs notably trading (13%) and driving (16%).

Farmers were trained to stay outside the area the spray takes place for 4 to 6 hours for the chemical mists and aerosols to dry before they can enter the farm. The present study observed that farmers and the farm owners stay in the farms throughout the period of the spraying activities thereby exposing them to the chemical concentrations in the area.

The results of the survey of the present work revealed that though spraying was done in the open area, the presence of tree canopies and the canopies of cocoa tree allow the accumulation of high chemical aerosol in the workplace thereby increasing the health risk level. The few spray men who have some knowledge of the chemicals toxicity try to follow the direction of the wind, but still complain of difficulties of identifying the sources of the wind.

DOSHWA (1990) has reported that breathing hazardous chemical mists / aerosol or eating and smoking with chemicals stained hands could pose health hazards. Novotny *et al*., (1998) associated a ten-fold increase in the risk of dying from chronic obstructive lung disease (asthma) with cigarette smoking. Thus, the twenty-one percent (21%) of respondents who smoke stand the risk of suffering from chronic asthma and other multiple exposures which could pose serious respiratory diseases and cancer to their health.

5.2 Laboratory Experiments.

According to results of the study done by USEPA (1994), most of the synthetic pesticides classified as hazardous by United States Environmental Protection Agency (USEPA), such as thimethoxam, bifenthrin and imidacloprid used for the control of diseases and pests of cocoa are neurotoxicants which often affect the central nervous system (CNS) (ATSDR, 2002a). The study also revealed that exposure to large amounts of these chemicals for short

periods adversely affects the human central system, the kidney, the liver, the lung and the heart, and are often characterized by light headed feeling USEPA (1994). The Agency for Toxic Substances and Disease Registry (ATSDR) also reported in 2001 that low to moderate levels of these chemicals can cause tiredness, weakness, memory loss, nausea, loss of appetite and drunken-type actions, loss of body weights, and skin and eye irritations. These symptoms were similar to those observed in this study were not different from the findings in this present study. Daily exposure of the rats showed varying signs of irritation, disturbed coordination, quietness followed by sleep and tremor when exposed to high concentrations of the bifenthrin and thiamethoxam.

The laboratory experiments revealed that high concentrations of the two chemicals used for the experiments affected the fur of rats. Itching was observed in the first two groups (high and medium concentrations) as the rats were seen biting their skins. A similar situation was also observed by Pauluhn *et al*., (1998) in human volunteers exposed for 1-hour period of bifenthrin at concentration approximately 0.1 mg/m3. This effect was also complained by the respondents of the present study.

From the results, the significantly lower body weights ($p \leq 0.05$) of rats exposed to bifenthrin and the thiamethoxam from high to low concentrations compared to the no chemically exposed group showed that exposure to high concentration of the chemicals could affect the weights of organisms. Once the target organs are affected, metabolic activities get disrupted, or the rats may be traumatized during the exposure, thus affecting their feeding rate which finally affects their proper body development. This observation was true for the present study.

The nervous system is the target organ of the toxic action of bifenthrin, but the effects on the respiratory tract can also be observed, such as massive haemorrhages and oedema of the lungs following inhalation of the chemical above the permitted concentrations as was observed by Soderlund *et al*., (2002). It must be noted that, these effects were not showed (plate c4) This exposes the farmers who use the permitted concentrations (30ml/16L of water and 17ml/16L of water of bifenthrin and thiamethoxam respectively) to lesser hazards than those who use above the permitted concentrations for the reason that higher concentrations are more effective as some farmers revealed.

The study further revealed that eye and skin irritations were the common complaints of the respondents. The clinical observations reported by World Health Organization (WHO) in 2005, and He *et al*., (1998) showed that bifenthrin and thiamethoxam cause skin and eye irritations as well as the nervous system which may lead to hypoactivity, ataxia, increased respiratory rate, and coma. Iregren *et al*., (1993) and Nelson *et al*., (1943) also reported that the critical effect of occupational exposure to these chemicals were seen in volunteers after few hours of exposure to bifenthrin.

The major histological findings occurred in the lungs of two rats that were exposed to high (0.51mg/kg) concentration of Actara (plate c4). The lungs serve as the main portal for the entrance of most hazardous chemicals. This observation explains the reason why most effects arising from exposure to environmental toxicants are mostly respiratory related.

The histological studies showed slight haemorrhage of the lungs coupled with inflammation after 8 weeks of exposure to high (0.51mg/kg) concentration of thiamethoxam. In a similar study by Green *et al*., (2005), involving rats exposed to thiamethoxam, his examination of animals that died revealed discolouration of the lungs, alveolar sac enlargement, haemorrhages, and oedema.

The incidence of certain tumours in the rats exposed to high concentration of thiamethoxam in the lungs over the duration was observed. This gives possible indication of carcinogenicity relevant for human assessment as was observed by Shukla *et al*., (2001) which the study supports.

Apart from the histopathological changes observed with the lungs high concentration of thiamethoxam, no exposure-related differences were detected in heart, lungs, kidney and the nervous system functions. A similar observation was made by He *et al*., (1988). This confirms the fact that thiamethoxam as a chemical for the control of diseases and pests of cocoa plant could be more harmful than the bifenthrin to humans who apply them, especially if the right concentrations are not used.

Recent studies carried out in the European Union and the United States have shown detectable amount of bifenthrin metabolites in urine samples, from the general population (Schettgen et al., 2002, Baker *et al*., 2001.) No evidence of adverse effects has been reported for such level of exposure. This confirms the tolerability of the compound in humans to some levels, which the present study also confirmed.

The present study also found no direct relationship between the concentration of the chemical bifenthrin and carcinogenicity associated. This is in keeping similar findings by IPCS (1993).

6.0 SUMMARY, CONCLUSION AND RECOMMENDATIONS

6.1 SUMMARY AND CONCLUSION

From the research conducted both in the field and in the laboratory with albino rats, it was observed that exposure to thiamethoxam with high concentration to control diseases and pests of cocoa plants can pose health hazards to the users either partly or throughout their life. This revelation came as a result of the development of tumour in two of the rats exposed to the chemical in the laboratory experiments. Bifenthrin on the other hand did not clearly indicate any toxicity on the rats. This is an indication that farmers working with bifenthrin could be safer than those working with thiamethoxam.

The major health complaints of farmers ranged from headaches (30%), skin irritation (24%), dizziness (14%), nose irritation (13%), eye irritation (7%), nausea (6%), throat irritation (3%) and diarrhea (2%).Dermal related diseases such as rashes, dry skin were prevalent.

Immediate symptoms often experienced after working with these chemicals (bifenthrin, thiamethoxam and imidacloprid) are throat irritation, itching, nausea, headaches and fatigue. Laboratory studies showed results consistent with National Institute for Occupational Safety and Health (1987) that the acute and sub-chronic effects of these chemicals on rats range from itching, breathing difficulties, fur removal, tremor in severe exposures and sleep.

In most workplaces (farms) visited, it was found that farmers seldom use respirators and other protective equipment and this increases the risk of exposure to toxic chemicals. The results of pathological studies also showed slight morphological changes in lungs of some

rats exposed to high (0.51mg/kg) concentration of thiamethoxam. The affected lungs showed slight tumour. The organs (lungs, liver, heart, and kidney) of the other concentrations including the concentrations of bifenthrin showed no noticeable symptoms of toxicity (plates). Although the approved chemicals cannot be completely free from any side effects, this study has shown that, overall, their effect on the users are tolerable and considered negligible as compared with systemic substances/compounds like Monocrophos (Azodrin), Dicrophos (Bidrin) and persistent organochlorine like DDT which are universally banned.

The use of the chemicals for the control of diseases and pests of cocoa plants by the farmers would continue to increase due to the enormous advantage chalked by the introduction of the mass-spraying of cocoa farms which has been introduced by the government. Practicing workplace hygiene and work education on handling and use of the pesticides as well as minimizing exposure through the use of personal protective equipment and clothing are simplest means of reducing the associated health effects of these toxic chemicals in the agriculture industry in Ghana.

6.2 RECOMMENDATIONS

1. The perception of the farmers on the harmful effects of the pesticides is not fully reflected in practices, and that attitudes and practices are inconsistent with each other. Various precautions need to be taken in order to bring about a consistent between the farmers' existing environmental awareness and their behaviour.
2. Farmers must adequately protect themselves from hazards associated with spray of cocoa plants by using appropriate protective clothing and equipment as well as any

appropriate technique to reduce exposure. Practicing workplace hygiene and education on handling and use of pesticides must be ensured by occupational health and safety personnel, the government and the CSSVD in order to avert the incidence of occupational related diseases.

3. Extensive education must be carried out by the Environmental Protection Agency, Occupational and Environmental Unit and NGOs on the risk associated with the handling, use and disposed of the chemical containers at the workplace to reduce the incidence of poisoning among the users in the environment.
4. Much more study on the effects of pesticides on non-target organisms should be undertaken by conducting regular tests such as Respiratory, Liver Function Tests, as well as field measurements of chemical concentrations/levels in the environment.
5. The availability and the use of Personal Protective Equipments by farmers should be ensured by the appropriate bodies such as the government, chemical manufacturers and sellers, since they are the most appropriate measures at which risks and hazards associated with the use of these chemicals can be controlled.
6. The effective methods to dispose of containers of the chemicals after use should be ensured to avoid environmental contamination.
7. Frequent health surveillance of farmers who work with these pesticides by Occupational and Environmental Health Unit (GHS/MOH) and Environmental Protection Agency (EPA) must be conducted, since that is important tool in preventing adverse health effects from hazardous chemicals. This should include biological monitoring (blood, urine or exhaled air), medical tests and examinations of farmers by Safety and Health physicians.
8. Government and the Ministry of Agriculture should ensure that farmers comply with the recommended concentrations of pesticides use.

9. Government and the Occupational and Environmental Health Unit (OEHU-GHS/MOH) together with EPA-Ghana must ensure the implementation of the ILO Recommendation 161, which envisages the formation of comprehensive occupational heath services in every country.

REFERENCES

Ajao, F. (2003) A study of the effects of chemical paints on the health of artisans Presented to the Department of Theoretical and Applied Biology, KNUST, Ghana 110pp

Aldridge, W. N., (1990) An assessment of the Toxicological Properties of pyrethroids and their Neurotoxicity. *Toxicology,* 21(2): 89-104

Anonymous (1990) Analysis of constraints on adoption of Crop Research Institute of Ghana (CRIG) recommendations in Offinso District: Results and Discussion. (C. P. Henderson and A. P. Jones ed.); 15pp. Cocoa Research Institute, Tafo, Ghana

Anonymous (1995).Report on causes of recent decline in cocoa production in Ghana and measures to revamp the industry. Office of the President, Accra: 103pp

Anonymous, (2001) the state of the Ghanaian Economy in 2000 Institute of Statistical, Social and Economic Research (ISSER), University of Ghana, Legon, 162pp

Astrand, I (1975) Uptake of solvents in the blood and tissues of man Scand J Work Environ Health 1: 199-218

Baker, S. B., Barr, D. B., Driskel, W. J., Beeson, M. D., Needham, L. L. (2001) Quantification of selected pesticide metabolites in human urine using isotope dilution high performance liquid chromatography / tandem mass spectrometry. J. Expo. Anal. Env. Epid., 10: 789-798

Bateman, D. N., (2000) Management of pyrethroid exposure *Journal of Toxicology* – clinical Toxicology, 38 (2):107-109

Bateman, M. J.(1988) Ghana Cocoa Pricing Policy study. Commodity information Inc. 1981: 77pp.

Bird, M, (1981) Industrial Solvents: some factors affecting their passage into and through

the skin. Ann Occup Hyg 24:235-244

Browning, E. (1965) Toxicity and metabolism of industrial solvents Amsterdam, the Netherlands: Elsevier Publishing Company

Chen S, Wu Y, He F (1991). Levels of exposure and biological monitoring of pyrethroids in spraymen. Br. J. Ind. Med., 48 : 82-86

Cohen, S., Klaunig, J., Patton, D., and Fenner-Crisp, P. (2003). The Human Relevance of Information on Carcinogenic Mode of Action. Overview. Crit. Rev. Toxicology 33, 581-589.

Department of Environmental and Occupational Medicine (DEOM) (2001). Dermatitis among workers exposed to metal working fluids. Liberty Safe Work Research Centre. Aberdeen, pp. 35-70.

Department of Occupational Health, Safety and Welfare (DOSHWA) (1990) Spray Painting national Occupation Health and Safety commission. Workers compensation and rehabilitation Commission. Western Australia 5 p, illus. http//www.nohsc.gov.an/

Department of Occupational Health, Safety and Welfare (DOSHWA) (1990). Spray painting, National Occupational Health, and Safety Commission. Workers Compensation and Rehabilitation Commission. Western Australia [5]p, illus. http://www.nohsc.gov.au

Dormon E. N. A (2006). From a technology focus to innovation development: The management of cocoa pests and diseases in Ghana pp 187-198.

Engstrom, K., Husman, K, Pfaffli p, and Riihimaki, V. (1978). Evaluation of occupational exposure to xylene by blood, exhaled air and urine analysis. Scand J Work Environ Health 4:114-121.

EXTOXNET (Extension Toxicity Network) (1998). Imidacloprid-Pesticide Information Profile. University of California-Daris, Oregon State University, Michigan State University, pp. 167-189.

Fischman, M. L. (1991). Proctor and Hughes' chemical hazards of the workplace. 3rd ed. New York, NY: Van Nostrand Reinhold.

Freeman, C., (1982) Acute oral toxicity in rats: FMC 54800. FMC study No. A83-859. DPR Vol. 50429-022, # 36650

Freud, E. H., Petithuguenin, P. and Jacques Richard (in press) the diffusion and impact of cocoa research themes in Ghana and Cote d'Ivoire proc. 12th Int. Cocoa Res. Conf., Salvador, Brazil, Bahia 17-23 Nov., 1996

Gerken, A., Suglo, J., & Braun, M.(2001) Crop Protection Policy in Ghana. ICP/MoFA, Pokoase, Ghana. 185pp

Gill and Duffus (1989) Cocoa Statistics. Gill and Duffus Gp. Ltd: 29pp.

Green, T., Alison, T., & Robert L., (2005) Thiamethoxam induced mouse tumours, part 1. Journal, volume 5, 10pp

Green, T., Richard, P.,Sara, L., Timothy, P., Case study : Weight of Evidence Evaluation of the Human health Relevance of Thiamethoxam-Related Mouse Liver Tumuors. (Published in February, 2005a)

Hayes, W., (1982) Pesticides studied in man. Williams and Wilkins, Baltimore, London, Occupational Health Services, Inc. "pyrethrum'' Material Safety Data Sheet. April, 1987. New York : OHS, Inc.

He F, Sun J, Han K, Wu Y, Yao P, Wang S, Liu L. (1988). Effects of pyrethroid insecticides on subjects engaged in packaging pyrethroids. Br. J. Ind.., 45(8) : 548-551

He F, Wang S, Liu L, Chen S, Zhang Z, Sun J. (1989). Clinical manifestations and diagnosis of acute pyrethroid poisoning. Arch. Toxicol. , 63 (1): 54-58

He, F., Sun, J., Han, K., Wu, Y., Yao, K Effects of pyrethroid insecticides on subjects engaged in packaging pyrothroids. Br. J. Ind. Med. 1988; 45; 548-51

Hooda, L. R and Hooser, S. B (2002). Toxicology of newer pesticides for use in dogs and cats. The Veterinary Clinics: Small Animal Practice. 32(2) : 455-467

IARC (International Agency on Research on Cancer) (1991) IARC Monographs on the evaluation of carcinogenic risks to humans. Occupational exposures in insecticides application, and some pesticides. Lyons, IARC (volume 53)

International Programme for Chemical Safety (IPCS) (2001) Environmental Health criteria 223: Neurotoxicity risk assessment for human health principles and approaches. Geneva, World Health Organization (WHO), IPCS

International Programme on Chemical Safety (IPCS) (1993) Bifenthrin. In: *pesticide Residues in Food.Evaluations* 1992.Part II-Toxicology. .Joint FAO/WHO Meeting on Pesticide Residues (JMPR), Geneva, World Health Organization (WHO/PCS 93. 34): 79-102

Iregren, A., Toomingas, A. and Wang, Z. (1993) Irritation effects from experimental exposure to n-butyl acetate Am J Ind Med 1993; 24:727-742

JMRA (Pest Management Regulatory Agency)(2001). Imidacloprid: Regulatory Notes. REG2001-11. Ottawa: Health Canada, PMRA, http://www.pmra-arla.gc.ca/english/pdf/reg2001-11-e.pdf

JMRA, 1995. Imidacloprid NTN (33893). Chapter 3: Impact on human and animal health. Draft

Kolmodin-Hedman B, Swensson A, Akerblom M (1982). Occupational exposure to some synthetic pyrethroids (permethrin and fenvalerate). Arch. Toxicol., 50(1) : 27-33

Le Quesne PM, Maxwell IC, Butterworth STG (1980). Transient facial sensory symptoms following exposure to synthetic pyrethroids. A clinical and electrophysiological assessment. (Neurotoxicology)., 2: 1-11

Leffler, C. T.(1999) Occupational asthma and contact dermatitis in a spray painter after introduction to an aziridine cross-linker. In: '' Environmental Health Perspectives, vol 107, No. 7 July 1999

McCarty, J. D. (1986) Combined chronic oral toxicity and oncogenicity study of FMC 54800 (Biphenate) 2 year feeding study in albino rats. FMC study No. A83-952 DPR vol. 50429- 022, # 36650

Meek, M., Bucker, J., Cohen, S., Dellarco, V., Hill, R., Lehman-McKeeman, L., Longfellow, D., Pastoor,T., Seed, J., and Patton, D. (2003). A Framework for Human Relevance Analysis of Information on Carcinogenic Modes of Action. Crit. Rev. Toxicol 33, 591-653

Muller-Mohnssen, H. (1999) Chronic sequelae and irreversible injuries following acute pyrethroid intoxication. *Toxicol*. Lett., 107 ; 161-176.

Mulye, H.S (1996). Supplementary review of imidacloprid technical and the end-use products, Admire 240F insecticide. Submission Numbers: 95-1229 and 96-2186. Environmental Assessment Division, PMRA, Health Canada.

Nelson, K. W., Ege, J. F. Jr., Ross, M., Woodman, L. E. and Silverman, L (1943) Sensory response to certain industrial solvent vapours J *Ind Hyg Toxicol* 1943; 25: 282-285

Novotny, T. E. and Giovino, G. A. (1998). Tobacco use. In: Brownson, R. C., Remington,

P.L., Davis, J.R. (ends). Chronic Disease Epidemiology and Control. Washington, DC: American Public Health Association, 1998. Pp 117-148.

Occupational and Environmental Health Unit (OEHU) (2002). A Handbook on occupational health. Ghana Health Service/Ministry of Health, Ghana.

Opoku, I. Y., Akrofi, A. Y. and Afrifa, A. A. (1997) The spread 107of *P. megakarya* on cocoa in Ghana : Proceedings of the 1st International Cocoa Pests and Disease Seminar, 6th to 10th November, 1995, Accra, Ghana pp. 98-107

Opoku, I. Y., Akrofi, A. Y., Appiah, A. A. and Luterbavher, M. C.(1998) Trunk injection of Potassium Phosphonate for the control of black pod disease of cocoa *Tropical science* (in press).

Pauluhn, J., Machemer L. H, (1998) Assessment of pyrethroid-induced paraesthesias: Comparison of animal model and human data Institute of Toxicology, Bayer AG, Wuppertal, Germany. Toxicol. Lett., Aug; 96-97 : 361-368

Reed, N. R. 1991 Bifenthrin (Captured 2 EC) Risk Characterization document. California Department of Food and Agriculture.

Riihimaki, V. Pfaffli, P., and Engstrom, K. (1978) Evaluation of Occupational exposure to xylene by blood, exhaled air and urine analysis. Scand J Work Environ Health 4: 114-121

Roberts, R (1999) Recognition and management of pesticide poisonings, 5th ed. Washington, DC, United States Environmental Protection Agency (Publication No. 735- R-98-003)

Schettgen, T., Heudorf, U., Drexler, H., Angerer, J., (2002) Pyrethroid exposure of the general population is this due to diet. Toxicol. Lett., 134 (1-3): 141-145

Shah, R. G J. Lagueux. Kapur, P. Levallois, P. Ayotte, M. Tremblay, J. Zee. And G. G. Poirier,

(1997). Determination of genotoxicity of the metabolites of the pesticides Guthion, Sencor. Lorox. Reglone. Daconil and Admire by P-Postlabeling Molecular and Cellular Biochemistry. 169; 177-184.

Shukla Y, Arora A, Singh A (2001). Tumourigenic studies on deltamethrin in Swiss albino mice. *Toxicology*, 163 : 1-9

Soderlund, D. M., Clark J. M., Sheets, L. P., Mullin, L. S., Piccirillo, V. J., Sargent, D., Stevens, J. T., Weiner, M. L., (2002) Mechanisms of pyrethroid neurotoxicity : implications for cumulative risk assessment. *Toxicology*, 171: 3-59

Tomlin, C. D. S (2000). The Pesticide Manual. Twelfth Edition. British Crop Protection Council, Survey, U.K

Tucker SB, Flannigan SA (1983). Cutaneous effects from occupational exposure to Fenvalerate. Arch.. Toxicol., 54 : 195-202.

United States Environmental Protection Agency (USEPA) (1994) Suplement to the 1986 EPA air quality criteria for lead volume 1, Addendum: Relationship of blood pressure to lead exposure. US Environmental Protection Agency, office of Health and Environmental Assessment (EPA/600 / 8-89/049F)

United States Environmental Protection Agency (USEPA) (1996b) Health Effects Test Guidelines OPPTS 870. 3465 Subchronic Inhalation Toxicity (‘’ Public Draft ‘’)

United States Environmental Protection Agency (USEPA), Office of Research and Development. EPA/712/C-96/204 Washington, DC

Waibel, H., (1994) Towards an economic framework of pesticides policy studies. In : Proceedings of the Gottingen workshop on pesticide policies. S. Agnes, G. Fliescher and H. Waibel (Eds). Gottinger Schriften Zur Agrarokonomie heft 66. Universitat

Gottingen, pp 1-10

World Health Organization (WHO) (1985). Nordic Council of Ministers; Oganic solvents and the central nervous system, EH5 Copenhagan, Denmark: World Health Organization and Nordic Council of Ministers, pp. 1-39

World Health Organization (WHO) (1999). Safety of pyrethroid-treated mosquito nets. Geneva, World Health Organization (WHO/CDS/CPE/WHOPES/99.5).

World Health Organization Pesticides Scheme (WHOPES) (2005). Safety of pyrethroids for Public Health, pp. 27-45

Zhang, Z., Sun, J., Chen, S., Wu, Y., (2002) Levels of exposure and biological monitoring of pyrethroids in spraymen Br J Ind. Med 48: 82-6

APPENDIX

Appendix A - Questionnaire

QUESTIONNAIRE TO ASSESS THE EFFECTS OF CHEMICALS ON THE HEALTH OF FARMERS WHO USE THEM FOR SPRAYING ON COCOA FARMS

1. Location:

……

2. For how long have you been spraying? 1 – 3 4 – 6

   7 – 9 10 and above

3. What are the types of chemicals you usually use?

……

……

4. What are the most common chemicals used for spraying on cocoa farms?

……

5. Why do you like using this particular kind of chemicals? ……

……

6. How do you mix the chemicals before use? ……

……

7. How many tanks of chemicals do you spray in a days?

……

……

8. a. Do you wear protective clothing when spraying? Yes NO

b. If yes, what kind (tick as applicable) coverall Hand Gloves

   Nose mask/respirators Goggles/face mask

Helmet/cap others (specify) ……..

c. If No, (why) explain

……

……

……

9. How often do you wear protective clothing? Always Not Always

10. How do you often wash your hands? After spraying

Before eating others (specify)……

……

11. What substance/chemical do you use for washing off the chemicals?

……

Detergent/soap Water Others Specify (Name)

12. a. Do you smoke? Yes No

b. If yes, when was the last time you smoked?

A year ago 2 years ago 3 years ago Daily

13. a. Do you drink alcohol? Yes No

b. How often? Daily once while

14. How often do you visit hospital for medical check up or drug/chemical shop? Daily weekly monthly quarterly

15. When was the last time you visited hospital?

……

16. Which of the following health problems do you frequently experience?

(Tick as appropriate)

Asthma Headache Dizziness Nausea

Eye irritation Nose irritation Throat irritation

Skin irritation

17. Do you itch after spraying? Yes No

18. a. Do you stay in the farm after spray? Yes No

b. If No, Why?

Comment

……

……

……

c. If Yes, why?

……

……

……

19. a. Do you have any skin disease? Yes No

b. If yes for how long?

……

20. a. Do you cough? Yes No

b. If yes, how often? Always Not always

c. How long have you been coughing? A year ago

2 years ago 3 years ago

21. Do you associate your health problems with the spraying?

Yes NO

22. a) What other work do you do apart from the spraying?

b) How long have you been doing this work?

……

23. Other comments

……

……

……

……

……

……

……

Appendix B - Statistical Analysis

1. Effect of Period of Pesticide Use on Health Hazards

Descriptives

Treatment	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	
					Lower Bound	Upper Bound			
2.00	5	38.4760	4.8406	2.1648	32.4656	44.4864	33.33	42.86	
5.00	5	43.3080	14.3217	6.4049	25.5252	61.0908	28.57	60.00	
8.00	5	41.6660	13.7442	6.1466	24.6003	58.7317	25.00	60.00	
11.00	5	66.6660	31.1814	13.9447	27.9492	105.3828	33.33	100.00	
Total	20	47.5290	20.5973	4.6057	37.8891	57.1689	25.00	100.00	

ANOVA

	Sum of Squares	df	Mean Square	F	Sig.	
Between Groups	2501.866	3	833.955	2.400	.106	
Within Groups	5558.895	16	347.431			
Total	8060.761	19				

* The mean difference is significant at the .05 level.

2. Effect of Use of Protective Clothing on Health Hazards

Descriptives

Treatment	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	
					Lower Bound	Upper Bound			
.00	5	69.6100	10.5661	4.7253	56.4905	82.7295	53.85	77.78	
.50	5	20.0000	27.3861	12.2474	-14.0044	54.0044	.00	50.00	
1.00	5	17.7380	13.3642	5.9766	1.1442	34.3318	.00	33.33	
Total	15	35.7827	30.1851	7.7937	19.0667	52.4986	.00	77.78	

ANOVA - HARZARDS

	Sum of Squares	df	Mean Square	F	Sig.	
Between Groups	8594.955	2	4297.478	12.394	.001	

Within Groups	4160.973	12	346.748			
Total	12755.928	14				

* The mean difference is significant at the .05 level.

3. Effect of ACTARA on Body Weight

Descriptives

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	
					Lower Bound	Upper Bound			
.00	6	7.5333	3.4471	1.4073	3.9158	11.1509	2.30	11.40	
.13	6	2.4000	2.2172	.9052	7.319E-02	4.7268	.00	5.00	
.26	6	.1333	5.5117	2.2501	-5.6508	5.9175	-6.80	10.00	
.51	6	-3.1000	3.3003	1.3473	-6.5635	.3635	-7.30	2.50	
Total	24	1.7417	5.3176	1.0855	-.5038	3.9871	-7.30	11.40	

ANOVA

	Sum of Squares	df	Mean Square	F	Sig.	
Between Groups	360.032	3	120.011	8.267	.001	
Within Groups	290.347	20	14.517			
Total	650.378	23				

* The mean difference is significant at the .05 level.

4. Effect of AKATE MASTER on Body Weight

Descriptives - WT_CHANG

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	
					Lower Bound	Upper Bound			
.00	6	8.1167	6.1496	2.5106	1.6630	14.5703	2.40	18.40	
.03	6	-8.3333E-02	1.9271	.7867	-2.1057	1.9390	-2.40	2.60	
.05	6	1.667E-02	.8010	.3270	-.8240	.8573	-1.00	1.10	
.10	6	-.9000	1.0020	.4091	-1.9515	.1515	-2.40	.50	
Total	24	1.7875	4.8427	.9885	-.2574	3.8324	-2.40	18.40	

ANOVA

	Sum of Squares	df	Mean Square	F	Sig.	
Between Groups	323.501	3	107.834	9.990	.000	
Within Groups	215.885	20	10.794			

* The mean difference is significant at the .05 level.

Appendix C