
Theses and Dissertations

Spring 2013

Building the case for residential herbicide exposure assessments in Iowa communities

Mark Gordon A. Lebeck
University of Iowa

Copyright 2013 Mark Gordon A. Lebeck

This thesis is available at Iowa Research Online: <http://ir.uiowa.edu/etd/2561>

Recommended Citation

Lebeck, Mark Gordon A.. "Building the case for residential herbicide exposure assessments in Iowa communities." MS (Master of Science) thesis, University of Iowa, 2013.
<http://ir.uiowa.edu/etd/2561>.

Follow this and additional works at: <http://ir.uiowa.edu/etd>



Part of the [Occupational Health and Industrial Hygiene Commons](#)

**BUILDING THE CASE FOR RESIDENTIAL HERBICIDE
EXPOSURE ASSESSMENTS IN IOWA COMMUNITIES**

by

Mark Gordon A. Lebeck

A thesis submitted in partial fulfillment of the requirements for the Master of Science
degree in Occupational and Environmental Health in the Graduate College of
The University of Iowa

May 2013

Thesis Supervisor: Assistant Professor T. Renée Anthony

Copyright by

MARK GORDON A. LEBECK

2013

All Rights Reserved

Graduate College
The University of Iowa
Iowa City, Iowa

CERTIFICATE OF APPROVAL

MASTER'S THESIS

This is to certify that the Master's thesis of

Mark Gordon A. Lebeck

has been approved by the Examining Committee
for the thesis requirement for the Master of Science
degree in Occupational and Environmental Health at
the May 2013 graduation.

Thesis Committee: _____
T. Renée Anthony, Thesis Supervisor

Hans-Joachim Lehmler

Matthew W. Nonnenmann

To Christy and Hayden,
for your unconditional love and overwhelming patience

ACKNOWLEDGEMENTS

I would like to thank my academic advisor, Renée Anthony, for your guidance, wisdom, patience, and understanding throughout this entire process. I will be forever grateful for your willingness to take me under your wing as your advisee.

I would also like to thank Hans Lehmler for providing me the unique research opportunity to work in your laboratory as a graduate research assistant. I am most appreciative of the skills gained from this experience under your tutelage, as well as the generous assistance I received from your research scientist, Iza Korwel.

Many thanks also to Matthew Nonnenmann for taking part in this process and the guidance you provided through our many conversations, as well as to former committee members Fred Gerr and Paul Romitti for having played significant roles at earlier stages of my research.

Of course all of this would not have been possible without the support and sustained encouragement from my family and friends, especially my wife Christy and son Hayden, who have been with me throughout this process every step of the way.

And finally, I must thank the many faculty and staff from the University of Iowa's College of Public Health and the Department of Occupational and Environmental Health, including the Environmental Health Sciences Research Center and the Heartland Center for Occupational Health and Safety. I am extremely grateful for the training and employment opportunities provided to me over these past years.

ABSTRACT

Pesticide use has steadily increased in the United States and throughout the world since the development of more highly effective agrichemicals dating back to World War II. While many of these compounds are considered to have little to no detrimental environmental impact with relatively low toxicity and potential for causing adverse health effects in humans, many recent studies examining the toxicological properties and health outcomes associated with exposure to a variety of pesticides suggest otherwise.

In heavily agricultural-based regions, particularly where row crops predominate, large amounts of herbicides and insecticides are used in activities involving pest management annually. The high volume of chemical applications to agricultural fields is cause for concern due their potential for leaching into soil following application events and subsequent transport to water systems. Pesticide-contaminated ground and surface water systems may pose a threat to public health by the presence and persistent elevated concentrations of chemicals found in both public and private drinking water. The herbicides atrazine and glyphosate are and have been the two most heavily applied pesticides in the U.S. Many studies have examined occupational exposures to these compounds and related health outcomes, yet very few have evaluated low-level exposures to more susceptible rural populations. This thesis will examine state-of-the-science behind atrazine and glyphosate, evaluate drinking water quality measurements in relation to herbicide usage estimates in Iowa, and finally, make recommendations for future atrazine and glyphosate exposure assessment studies in rural Iowa populations.

TABLE OF CONTENTS

LIST OF TABLES vi

LIST OF FIGURES vii

CHAPTER

I. INTRODUCTION.....1

 Glyphosate2

 Atrazine.....3

 Pesticide Exposure – Health Outcome Studies4

 Laboratory Detection Methods – Exposure Assessment7

 Population-based Exposure Studies9

II. ENVIRONMENTAL PESTICIDE MONITORING AND USAGE ESTIMATES.....13

 Introduction.....13

 Exposure Pathways14

 Federal and State Databases for Water Quality14

 Pesticide Use Monitoring.....17

 Methods.....19

 Analyses20

 Results.....22

 Discussion.....24

 Conclusion27

III. CONCLUSION.....37

APPENDIX: SCATTER PLOTS.....40

REFERENCES50

LIST OF TABLES

Table 1: Atrazine exposure pathways studies	32
Table 2: Iowa SDWIS summary statistics by crop reporting district, 1990-2012	34
Table 3: Iowa SDWIS atrazine measurements by drinking water source, 1990-2004	35
Table 4: Linear regression of atrazine application as a function of year, 1990-2004.....	35
Table 5: Linear regression of atrazine concentration as a function of year, 1990-2004....	36
Table 6: Iowa SDWIS quarterly atrazine measurements, 1990-2012.....	36

LIST OF FIGURES

Figure 1: Herbicide use, U.S. agricultural market sector, 1987-2007 estimates	12
Figure 2: State-wide Iowa SDWIS measurements and annual atrazine usage, 1990-2004	30
Figure 3: South central CRD SDWIS measurements and annual atrazine usage, 1990-2004	31
Figure A1: Herbicide use, U.S. agricultural market sector, 2001-2007 estimates.....	41
Figure A2: Central Iowa CRD, atrazine usage and percent detected	41
Figure A3: Central Iowa CRD, atrazine usage and concentration measurements	42
Figure A4: East Central Iowa CRD, atrazine usage and percent detected.....	42
Figure A5: East Central Iowa CRD, atrazine usage and concentration measurements	43
Figure A6: North Central Iowa CRD, atrazine usage and percent detected	43
Figure A7: North Central Iowa CRD, atrazine usage and concentration measurements...	44
Figure A8: Northeast Iowa CRD, atrazine usage and percent detected.....	44
Figure A9: Northeast Iowa CRD, atrazine usage and concentration measurements	45
Figure A10: Northwest Iowa CRD, atrazine usage and percent detected.....	45
Figure A11: Northwest Iowa CRD, atrazine usage and concentration measurements	46
Figure A12: South Central Iowa CRD, atrazine usage and percent detected	46
Figure A13: Southeast Iowa CRD, atrazine usage and percent detected.....	47
Figure A14: Southeast Iowa CRD, atrazine usage and concentration measurements	47
Figure A15: Southwest Iowa CRD, atrazine usage and percent detected.....	48
Figure A16: Southwest Iowa CRD, atrazine usage and concentration measurements	48
Figure A17: West Central Iowa CRD, atrazine usage and percent detected	49
Figure A18: West Central Iowa CRD, atrazine usage and concentration measurements..	49

CHAPTER I

INTRODUCTION

Use of synthetic carbon-based chemicals for pest management purposes continues to increase throughout the world. While production and usage of many earlier, “first generation” pesticides has ceased, due in part to their ineffectiveness, environmental persistence, and toxicity, advancements in science and agriculture have led to the development of more effective and less toxic pesticides. The objectives of this chapter are to (1), review background and usage patterns of the herbicides atrazine and glyphosate, (2) review atrazine and glyphosate-related human exposure – outcome studies as well as animal toxicological studies, and (3) examine the state-of-science surrounding risk of exposure to these herbicides.

An estimated 857 million pounds of conventional pesticides, primarily herbicides and insecticides, were applied in the United States in 2007 with a majority (80%) used for agricultural purposes (Grube, 2011; Kiely *et al.*, 2004). Nearly one third of all pesticides applied to crop fields include the herbicides glyphosate and atrazine. Usage of glyphosate, the active ingredient in commercial formulations such as Roundup®, has steadily increased over the past twenty-five years (Figure 1). Following the 2000 planting season, glyphosate surpassed atrazine as the primary herbicide used in the agricultural market sector (Grube, 2011). The National Agriculture Statistics Service (NASS) in 2007 estimated that over 226 million acres were treated with herbicides in the United States and nearly 91 million acres were treated with chemicals for the control of insects (USDA, 2007). In Iowa alone, almost 20 million and 7.7 million acres were treated with herbicides and insecticides, respectively (USDA, 2007), accounting for

nearly 77% of Iowa's total geographic area. Widespread use of pesticides in Iowa is cause for concern due to their potential impact on human health and the environment.

Glyphosate

Glyphosate has become the dominant herbicide worldwide since its introduction in 1974 (Duke and Powles, 2008; Franz *et al.*, 1997). Glyphosate is an inexpensive and highly effective broad-spectrum herbicide that selectively targets 5-enolpyruvyl-shikimate-3-phosphate synthase and is considered by the United States Environmental Protection Agency (EPA) to have minimal detrimental effects on the environment. In short, glyphosate has little potential for being transported to groundwater systems due to its soil adsorption properties and susceptibility to degradation by soil microbes as well as its tendency to demonstrate little to no accumulation in aquatic systems. One important reason for the commercial success of glyphosate is the introduction of transgenic (genetically engineered), glyphosate-resistant crops in 1996 (Franz *et al.*, 1997). Currently, 90% of all transgenic crops grown worldwide are glyphosate resistant, and the adoption of these crops continues to increase annually. Global estimates from the years 1998-2003 suggest adoption rates of glyphosate-resistant crops at over 12 million additional acres per year (Dill, 2005).

Glyphosate is converted to aminomethylphosphonic acid (AMPA) by microbial degradation in soil (Franz *et al.*, 1997) and in plants (Reddy *et al.*, 2008), and both compounds have been detected in water streams in the United States (Battaglin *et al.*, 2005; Kolpin *et al.*, 2006). The median half-life of glyphosate in soil has been determined to range from 2 – 197 days (Giesy *et al.*, 2000). In agricultural fields, the half-life of glyphosate has been estimated at 47 days (Vencill, 2002), and its persistence

is dependent upon climatic as well as soil conditions (Tomlin, 2006). Considered stable to chemical and photodegradation, glyphosate adsorbs readily to soil, which suggests a low potential for contaminating groundwater (USEPA, 2012b). However, because the median half-life in water is estimated to be between 4 – 91 days with minimal photodegradation, and its estimated median soil half-life, the potential for surface water contamination exists due to soil erosion and runoff as well as from aquatic glyphosate applications (Tomlin, 2006). Glyphosate is poorly metabolized as evidenced by low absorption in animal studies and is rapidly excreted (from 1 – 5 days) as the parent compound in the urine and feces of rodents and humans (Williams *et al.*, 2000).

Atrazine

The most studied of the triazine herbicides, atrazine, was first registered with the EPA for use in 1958, and by the late 1990s, was the single most heavily applied pesticide in the United States (USEPA, 2012b). Perhaps the most recognizable of the triazine class of herbicides, atrazine is a pre- and post-emergent herbicide used to control broad-leafed weeds and some annual grasses. The herbicidal mechanism of atrazine involves the inhibition of photosynthetic electron transport in certain plants (Barr, 2008). The half-life of atrazine in soil and water is estimated to range from 13 – 261 days and 60 – 100 days, respectively. Due to its environmental persistence and high usage patterns, atrazine is the most commonly detected pesticide in surface water and is frequently detected in groundwater systems (USEPA, 2012b).

Atrazine is a form of the N-alkyl substituted 2,4-diamine of chlorotriazine and is metabolized via the glutathione detoxification pathway or by simple dealkylation. For glutathione detoxification, the chlorine atom on the triazine herbicide is subject to an

enzymatic-catalyzed substitution by the free sulfanyl (–SH) group on the internal cysteine residue of the glutathione tripeptide. The terminal peptides are enzymatically cleaved and the cysteine is N-acetylated. Although dealkylated metabolites can also be formed, atrazine mercapturate was identified as a major human metabolite of atrazine. The mercapturate and dealkylation metabolites are removed by way of urinary excretion.

Pesticide Exposure – Health Outcome Studies

Pesticides have been associated with a variety of adverse health outcomes, including attention deficit hyperactivity disorder-like behaviors (Sagiv *et al.*, 2010), contributing to increased risk of prostate cancer (Ritchie *et al.*, 2003), as well as increased risk for acute myocardial infarction and type-2 diabetes (Schreinemachers, 2010). The leading cause of infant mortality in the United States is birth defects, and there is increasing evidence that agricultural exposures may contribute to their occurrence (Bell *et al.*, 2001; Croen *et al.*, 2001; Garry *et al.*, 2002; Kristensen *et al.*, 1997; Munger *et al.*, 1992; Weselak *et al.*, 2008). In ecologic and cross-sectional studies, fetal growth and congenital abnormalities—including neurologic, circulatory, musculoskeletal, and respiratory defects—have been associated with inhalation and dermal exposures of pesticides or with levels of pesticides in local drinking water sources (Garry *et al.*, 1996; Stillerman *et al.*, 2008; Winchester *et al.*, 2009).

Triazine compounds have been linked to harmful reproductive effects including miscarriage and pre-term delivery (Arbuckle *et al.*, 2001; Savitz *et al.*, 1997) and can act as endocrine disruptors (Colborn *et al.*, 1993; Cooper *et al.*, 1996; Cooper *et al.*, 2000; Hayes *et al.*, 2003; Kniewald *et al.*, 2000; Rodriguez *et al.*, 2005). Atrazine in particular is an endocrine disruptor (Colborn *et al.*, 1993; Cooper *et al.*, 1996) and has been

associated with increased risk for birth defects, including pseudopregnancies stemming from disruption of ovarian function and resultant changes to the endocrine profile of the female. In a nationwide study, Winchester found that total birth defects increased among children conceived during the months of April – July, and atrazine concentrations in area surface water were directly correlated with increased odds of all birth defects ($p < 0.001$) (Winchester *et al.*, 2009). Munger found that atrazine in surface water sources was significantly associated with intrauterine growth retardation (Munger *et al.*, 1997).

Several studies evaluating farm chemical mixing and application activities suggest that glyphosate exposure may also lead to endocrine disruption (Dallegrave *et al.*, 2003; Lin and Garry, 2000; Mesnage *et al.*, 2009; Savitz *et al.*, 1997). Commercial glyphosate formulations, such as Roundup®, are considered to be of low toxicity (Bradberry *et al.*, 2004). However, recent findings suggest that exposures to glyphosate-based herbicides used for both commercial and domestic purposes may affect human reproduction and fetal development, possibly by the inhibition of the enzyme aromatase thus blocking the conversion of androgens into estrogens (Benachour *et al.*, 2007; Richard *et al.*, 2005). Dallegrave found that glyphosate was toxic to Wistar rats, inducing developmental fetal retardation (Dallegrave *et al.*, 2003). Farmers' dermal and inhalation exposures to glyphosate from mixing and application activities has been associated with increased risk of miscarriages and premature birth (Savitz *et al.*, 1997). There may also be a link between glyphosate exposure and an increased risk for birth defects including orofacial clefts. From surveillance conducted in 14 states between the years of 2004 and 2006, the Centers for Diseases Control and Prevention (CDC) National Birth Defects Prevention Network (NBDPN) estimated the prevalence of cleft lip (with or without cleft

palate) and cleft palate only at 1.1/1000 live births and 0.64/1000 live births, respectively (NIDCR, 2010). Causes of orofacial clefts are still poorly understood though they are suspected to occur as a result of genetic (Murray, 2002) and/or environmental factors (Bouvier *et al.*, 2006; Pellizzari *et al.*, 2003; Quackenboss *et al.*, 2000).

Many population-based epidemiologic studies have retrospectively examined for an association between orofacial cleft outcomes and pesticide exposure. A recent comprehensive meta-analysis examined 19 studies and further suggest an association between maternal pesticide exposure and risk of orofacial clefts (Romitti *et al.*, 2007). Exposure to specific types of pesticides or to amounts used was not included with the analysis that involved assessments based on study participant interview response (e.g. YES/NO/MAYBE to pesticide exposure and agricultural work) and industrial hygienist review of participant's reported exposures.

Animal studies that have involved other pesticide treatments to developing embryos during early gestation in pregnant mice indicate increased occurrences of orofacial clefting (Courtney and Moore, 1971; Hood *et al.*, 1979; Tian *et al.*, 2005). A recent animal study examined the effects of glyphosate and glyphosate-based herbicides (GBH) on the development of *xenopus laevis* (African clawed frog) embryos. Two separate amounts of pure glyphosate at 360 picograms (pg) and 500 pg were injected into the embryos. Additionally, embryos were treated with three dilutions of GBH/modified Barth's saline (1/3000, 1/4000, and 1/5000). Results suggest an association between glyphosate/GBH exposure and alterations of retinoic acid (RA) signaling (Paganelli *et al.*, 2010). Induction of craniofacial malformations may be a result of increased RA (Sulik *et al.*, 1988) and sonic hedge hog (*shh*) signaling combined with altered expression

of the orthodenticle homeobox 2 (*otx2*) gene and resultant defects in cranial neural crest cells (Paganelli *et al.*, 2010). While the sublethal doses used in the Paganelli study may resemble potential environmental exposure concentrations experienced by susceptible human populations, investigators examined adverse outcomes in an amphibian species as a result of exposure by direct injection or treatments of the herbicide to the developing embryos. Pathways and routes of exposures in humans would originate from other sources: for example, ingestion of contaminated water and food or perhaps through inhalation resulting from airborne drift as a result of application events.

The large-scale agricultural glyphosate use together with these toxicological findings raise concerns about low level glyphosate exposure in susceptible farming and rural populations. Unfortunately, little is known about the prevalence of glyphosate exposures in rural populations, as biomonitoring studies have primarily examined occupational exposures during application events and were unable to assess low-level environmental exposures over time (Baronti *et al.*, 2000; Kolpin *et al.*, 2002).

Laboratory Detection Methods – Exposure Assessment

Pesticide exposure assessment studies often include analysis of environmental and biologic samples. Environmental sampling matrices may include water or soil, indoor house dust collected by specialized vacuum procedures and surface wipes, as well as indoor/outdoor air collected by active or passive monitoring techniques. Typical biologic matrices collected in biomonitoring studies include urine, saliva, and blood. Pesticides and their degradates are then extracted from their respective environmental or biologic matrix, oftentimes requiring additional derivatization steps before analytical detection methods are used for identification and quantification purposes. Environmental pesticide

concentrations and estimates of exposure may then be determined by resulting data generated from these analyses.

Traditional solvent extraction techniques used for pesticide recovery and isolation from their respective sample matrix can be time- and resource-intensive, including volume of solvent, duration of optimal sonication or mixing, and the number of required extraction steps (Picó *et al.*, 2007). Recent developments in extraction methods such as solid-phase micro-extraction (SPME) are beginning to supplant these methods as they demonstrate enhanced sensitivity, are not as expensive, and can be effective in high-throughput analytical settings (Picó *et al.*, 2007; Theodoridis *et al.*, 2000). The higher concentrating efficiency of SPME, limited usage of organic solvents and thus eliminating the need for transfer of organic solvents to chromatography systems, as well as utilization of smaller sample volumes are a few advantages compared to traditional extraction techniques. With these enhancements have come lower limits of detection and quantification, which in turn may help to strengthen pesticide exposure assessments.

A significant challenge investigators face in the chemical analysis of biologic and environmental samples involves the required enhanced sensitivity of the chromatography instrument and its capacity to detect many analytes that are matrix-specific. This may require optimization in calibration standard preparations in order to quantify observed analytical responses (Poole, 2007). Method limits of detection and quantification vary by assay and target compound when employed for exposure assessment purposes (Biagini *et al.*, 2004). Gas chromatography (GC) and liquid chromatography (LC) techniques can be coupled with a variety of detection modes. GC methods, in conjunction with mass selective (MS) detection, have been reported for the analysis of glyphosate and its

metabolites from biologic and environmental matrices which ultimately require analysis of more stable compounds by employing intermediate derivatization steps (Borjesson and Torstensson, 2000; Motojyuku *et al.*, 2008). GC and LC methods have been used to detect atrazine and other parent triazine compounds and their metabolites in human urine (Mendas, 2000; Olsson *et al.*, 2004) utilizing MS and nitrogen-selective electron capture detection as well as differing chemical extraction techniques.

Population-based Exposure Studies

Farmers who self-apply pesticides and commercial pesticide applicators may be at risk for occupational exposures to many agrichemicals (Bouvier *et al.*, 2006; Curwin *et al.*, 2005a; Curwin *et al.*, 2005b; Curwin *et al.*, 2007; Golla, 2007; Rodriguez *et al.*, 2005; Weselak *et al.*, 2008). In addition, rural populations that are not pesticide applicators, especially children, may be at greater risk of exposure to pesticides through contaminated water supplies, take-home chemical residues, contaminated soil and airborne drift as a result of application events (Eskenazi *et al.*, 1999). In the Workers' Family Protection Act of 1992 the U. S. Congress acknowledged concern about take-home exposures of hazardous chemicals transported from the workplace into the homes of workers (NIOSH, 2002). Studies have shown that in-home pesticide levels are significantly greater for farm versus non-farm homes (Curwin *et al.*, 2005a; Simcox *et al.*, 1995). A study of Iowa farmers conducted in the spring and summer of 2001 found that the families of farmers who self-applied the herbicide atrazine to their farm fields had higher urine atrazine metabolite levels than non-farmers or farmers who did not apply the herbicide themselves (Curwin *et al.*, 2005b; Curwin *et al.*, 2007). In a study of Iowa farmers who specifically applied atrazine, Golla found that the levels of atrazine in vacuumed house dust and

atrazine metabolites in the urine of family members increased with amount of atrazine applied on the farm (Golla, 2007). Golla also found detectable atrazine in vacuumed home dust samples and atrazine metabolites in the urine of farm families six months after atrazine was last applied on their farms. These studies demonstrate concern for long-term environmental exposure of farmers and their families to herbicides. Also, because of their close proximity to farm fields, non-farming families who reside in rural agricultural communities may also be at risk of long-term environmental herbicide exposures. If exposure to some herbicides is associated with risk for adverse health effects, then families at higher risk of exposure to herbicides would also be at increased risk of having children born with adverse health outcomes.

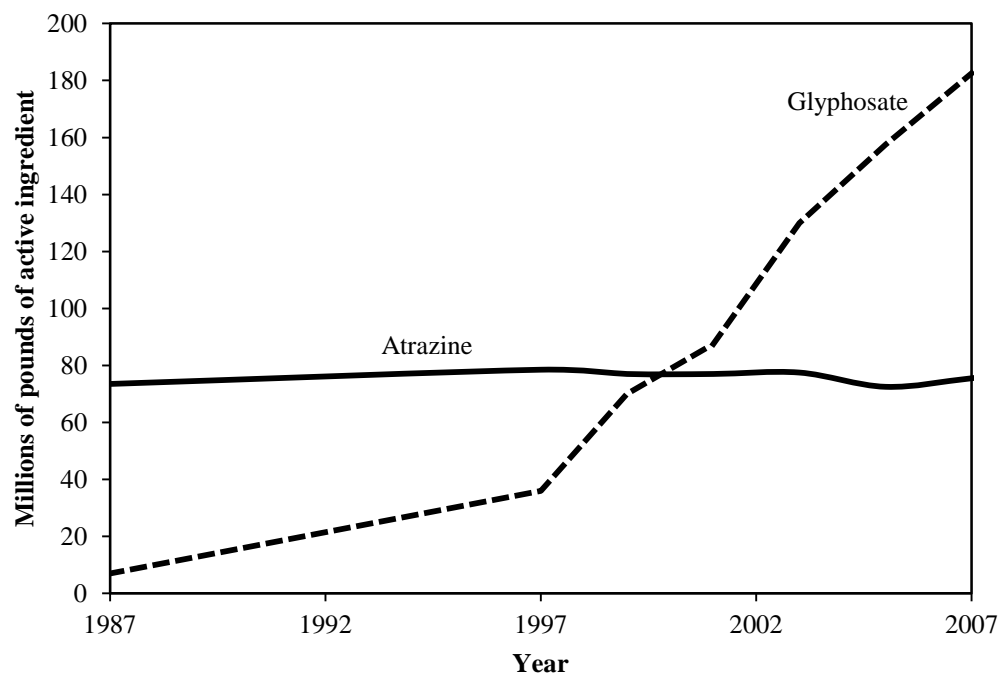
While there remains an unclear causal pathway between low-level, chronic exposures to pesticides and certain adverse health outcomes, the potential for pesticide exposure is of great concern particularly in areas where large amounts of agrichemicals are applied each year. Concerns about water system contamination by a variety of organic compounds and their effect on wildlife and human reproductive and developmental health by endocrine disruption are growing as monitoring evidence suggests their persistence in water supplies utilized for public and private drinking water. While analytical detection methods continue to develop increasingly sensitive exposure assessment tools, and with increasing pesticide usage patterns, further more comprehensive studies examining this potential exposure pathway are warranted.

Rural populations may be at greater risk of exposure to pesticides from contaminated water supplies, both municipal and private. The ground and surface water sources that supply many rural municipalities and private wells are in close proximity to

agricultural fields where pesticides are applied each year, thus increasing the potential for contamination by these chemicals. Pesticides may also contaminate groundwater supplies through inadvertent drainage from septic system effluent, or in more susceptible areas without developed sewer systems. While municipal water systems have been required to monitor their water quality, periodic testing for pesticides becomes less frequent when there is no evidence of contamination. Owners and users of private wells are not required to monitor their water sources, though there is additional evidence suggesting contamination in private well water sources (Kross *et al*, 1990).

In light of varying degrees of evidence suggesting rural populations are potentially exposed to herbicides by consumption of contaminated drinking water, existing historical pesticide monitoring data should be evaluated to assess contaminate levels in relation to agrichemical usage patterns. This would identify regions for future exposure assessment studies. Due to existing regional differences in types and amounts of pesticides applied for agricultural purposes, future studies may more effectively examine pathways and routes of exposure coupled with more sensitive analytical methods for more reliable quantification of exposure.

Figure 1: Herbicide use, U.S. agricultural market sector, 1987-2007 estimates



CHAPTER II

ENVIRONMENTAL PESTICIDE MONITORING AND USAGE ESTIMATES

Introduction

The presence of agrichemicals in aquatic environments, including surface water and groundwater systems, may have a detrimental impact on water quality (Kolpin *et al.*, 2002). Due to the increasing demand for groundwater, there may be increased potential for pesticide-contaminated surface waters contributing to depleted groundwater systems, especially where high capacity wells are in close proximity to surface waters.

The United States Environmental Protection Agency (EPA) considers triazine herbicides, including atrazine, to be endocrine disrupting chemicals (EDCs), capable of interfering with animal hormonal processes and developmental regulation (USEPA, 2012b). EDCs are used by private consumers and industry, and the National Research Council (NRC) has determined that industrially produced compounds with endocrine disrupting activity also include polychlorinated biphenyls (PCBs), plasticizers, food additives, oral contraceptives, herbal supplements, and beauty products as well as natural occurring compounds such as sex steroids, phyto-estrogens and heavy metals (NRC, 1999). EDCs may be found in agricultural run-off as well as wastewater from domestic and industrial sources. Because of their environmental persistence, low concentrations of EDCs have been detected in surface and groundwater used as a source for water supply with trace amounts detected in finished tap water (Baronti *et al.*, 2000; Ternes *et al.*, 1999a; Ternes *et al.*, 1999b).

Exposure Pathways

Exposure to pesticides can occur from a variety of different sources and by many pathways (Table 1). People who reside in rural areas may potentially be at higher risk of exposure from a variety of pathways, including airborne drift from application events, occupational-related activities such as mixing and applying pesticides, pesticide contaminated food supplies, and exposure to pesticide residues found in dust. Recent studies have evaluated multiple pesticide exposure pathways and results from several studies have consistently suggested that contaminated water supplies are a viable pathway for potential pesticide exposures.

For decades, federal and state governmental programs have been developed and used to monitor water quality throughout the U.S. in order to identify and quantify potential biologic and chemical contaminants found in finished and unfinished municipal drinking water systems. Raw groundwater and surface water sources, such as aquifers, wells, lakes, rivers, and streams have also been included with these monitoring efforts, particularly in areas that apply pesticides for agricultural purposes. Other governmental surveillance programs report annual pesticide usage data based on regional and local estimations to evaluate types and quantities of pesticides being applied. Together, these data sources can provide useful information for the evaluation of potential areas of concern related to pesticide exposures by susceptible populations.

Federal and State Databases for Water Quality

The Safe Drinking Water Act (SDWA) of 1974 authorized the EPA to set drinking-water standards for the protection of tap water quality in the United States (USEPA, 2012a). The SDWA also required that municipal water systems comply with

these standards while giving state and local agencies the responsibility for establishing effective controls to attain these standards. EPA has established maximum contaminant levels (MCLs) for water contaminants that may be conveyed to any user or public water system. While MCLs are typically enforceable standards, public systems may be granted compliance flexibility if there is no unreasonable risk to public health. Maximum contaminant level goals (MCLGs) are established for contaminants in drinking water below which there is no known or expected risk to human health. MCLGs incorporate a margin of safety and are non-enforceable public health goals (USEPA, 2012a). Due to available water treatment options and compound-specific analytical detection methods, regulatory MCLs are set as close to MCLGs as possible.

The EPA has set both the MCLG and MCL at 0.003 mg/L (3 ppb) for atrazine and 0.7 mg/L (700 ppb) for glyphosate. This suggests that there are no significant limitations in treatment technologies or the analytical tools required for detection and quantification of these compounds. The SDWA requires the EPA to periodically review the national primary drinking water regulations: the MCLs and MCLGs for both atrazine and glyphosate have remained constant since 1992 and 1994, respectively, indicating established levels are still considered protective of human health.

The EPA compiles monitoring data for drinking water contaminant measures in the Safe Drinking Water Information System (SDWIS) database. The SDWIS was established in order to allow the EPA to oversee state drinking water programs, track contaminant levels, respond to public inquiries, and prepare national drinking water quality reports. The responsible participating state agencies are required to report results of contaminant testing tap water data considered non-compliant (e.g. contaminant MCLs

exceeded). The SDWIS also allows the EPA to evaluate testing frequencies and subsequent contaminant levels such that they determine whether new regulations are needed for protection of human health (USEPA, 2012a). Over 172,000 municipal water systems are included in the SDWIS serving an estimated 90% of the U.S. population (USEPA, 2012a). The standards used for the determination of contaminant level violations, uniform protocols for data collection and management, and the laboratory certification program are strengths of the SDWIS. Laboratories participating in the SDWIS analyze water samples for contaminants according to EPA-approved methods. A significant limitation of SDWIS may be found in its lack of information on actual levels of contaminants of interest which may be reported only in situations of non-compliance. Monitoring is initially performed quarterly for atrazine and glyphosate. Following four consecutive quarters of no detections or if MCLs are not exceeded, public water systems (PWSs) are required to test annually for three years. After three years with no detections or detections below the MCL, PWSs may continue to test annually for the remainder of the compliance period and then apply for a six-year waiver should there be no history of detections or MCL violations for the contaminants of interest. Low-level pesticide exposures to populations served by these water systems may have the potential to go unchecked. The protection of public health and improvements to understanding health-related events may be better served by more comprehensive data recording and reporting regardless of compliance status.

The Iowa Department of Natural Resources (IDNR) conducts state-wide water quality programs, including management of Iowa's SDWIS program where all SDWA data for the state is recorded. The surface water monitoring program performs field

surveys and analyzes surface water quality for many of Iowa's rivers and lakes, including public recreation areas. The IDNR's interactive mapping program incorporates surface water monitoring results with pesticide sales density estimations reported by registered pesticide dealers across the state (IDNR, 2010). Monitoring results for 17 pesticides are reported by total number of detections over 5-year categories while sales densities are based on pesticide sales estimates within a 30-mile radius from each pesticide dealer's location. Surface water monitoring for atrazine and glyphosate began in 1990, and while it continues for atrazine, monitoring of glyphosate stopped after 2004. Annual sales estimates have been compiled for both atrazine and glyphosate since 1989.

Pesticide Use Monitoring

In addition to contaminated ground water and surface water monitoring data, U.S. federal and state agencies have developed surveillance programs for the evaluation of the types and amounts of pesticides applied for commercial and domestic purposes.

For over 220 years agricultural surveys have been conducted in the U.S. in effort to characterize the agriculture market sector. Specific components of these surveys involve evaluations of land value, crops, yields, livestock prices, and taxes. The first Census of Agriculture was performed in 1840 and provided a national inventory of agriculture-based production as well as state and territorial-based estimates. In 1863, the National Agricultural Statistics Service (NASS) was born when the United States Department of Agriculture (USDA) established a Division of Statistics (USDA, 2008).

Today, the USDA releases the Census of Agriculture every five years, providing extensive agricultural data for all states and counties in the United States. The most current census available is from 2007, with the 2012 census set to be released in February

of 2014. Information collected as part of each census now includes production expenditures and product market value estimates as well as characteristics of farming and ranching operations, such as size and types of production. Also included with each census are reports for agricultural fertilizer and pesticide usage as well as numbers of farms and acres treated with certain types of chemicals, however, specific compounds (e.g. active ingredients) are not included with this data.

Since 1979, the EPA has generated annual pesticide industry sales and use reports as a component of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) regulatory programs (Grube, 2011; Kiely *et al.*, 2004). These reports, when used in conjunction with the USDA's NASS agricultural census reports, may provide pesticide-specific usage indicators at the local level.

Iowa's Department of Agriculture and Land Stewardship (IDALS) has grouped the 99 Iowa counties into nine Crop Reporting Districts (CRDs). These groupings represent divisions of approximately equal geographic size with similar soils, growing conditions and types of farming. The compilations of many agriculture-based data are reported by CRD to summarize data at a district level and weight districts together by production percentages to arrive at state estimates.

While pesticide water monitoring and surveillance systems continue to support federal, state, and local aims of increased protection to public health and the environment, evidence of contamination to public water systems by detectable pesticide residues alone may not be sufficient to effect change to statutes and regulations that may control acceptable concentration levels of these contaminants. Further studies evaluating the health outcomes associated with similar exposures to these chemicals must continue to

help shape decisions made related to on-going risk assessments. These data are limited as indicators of contamination to water sources as well as public and private water systems, yet pesticide usage estimations may help to guide investigators and regulatory agencies in evaluating potential areas of concern due to quantities and types of pesticides being applied,

The objective of this study is to demonstrate a link between groundwater and surface water herbicide contaminant concentration levels and regional herbicide application estimates as an indicator for identifying areas of concern and susceptible populations when designing future herbicide exposure assessment studies in rural Iowa communities.

Methods

All SDWIS data for Iowa testing locations were received from the Iowa Department of Natural Resources, Water Supply Operations Section, in a series of queries from the state SDWIS database (Frank, 2012). The complete database included finished tap water measurements from 1,343 SDWIS municipal drinking water systems located throughout Iowa representing all 99 counties.

Information included with each data set were public water system name and the SDWIS participating facility identifier from which water was sampled, collection date, chemical analyte tested (glyphosate, atrazine and the atrazine breakdown products des-ethylatrazine and des-isopropylatrazine), testing results (concentration in mg/L), the analytical method employed and corresponding limit of detection (LOD) as well as the analytical laboratory's identifier. For another test, the drinking water source was categorized by one of six principle components: ground water (GW), purchased ground water (GWP), ground water under the direct influence of surface water (GU), purchased

ground water under the direct influence of surface water (GUP), surface water (SW), and purchased surface water (SWP).

Census of Agriculture data were retrieved from the NASS on-line database for the available census years of 1992, 1997, 2002, and 2007 (USDA, 2007). Herbicide application data were analyzed at the county level (“Fertilizers and Chemicals Applied”, then “Chemicals used to control-Weeds, grass, or brush”) with additional annual atrazine- and glyphosate-specific state-wide data examined for the years 1990-2006 using the NASS QuickStats ad-hoc query tool. Included with this data was percent of treated acres, number of applications, active ingredient/application (pounds/acre), active ingredient/year (pounds/acre), and total active ingredient (thousands of pounds/year).

Iowa CRD data were retrieved from the IDALS Iowa Pesticide Sales Database (IDALS, 2010). Application data included annual pounds of herbicide applied in each district and pounds of herbicide applied per acre of corn for the years 1990 – 2004. Statewide application measurements were tabulated from all CRD usage estimates for each year.

Analyses

Statistical analyses were performed using Microsoft Office Excel (Excel Version 2010). SDWIS data was sorted by county, herbicide, and measurement date. Each county was categorized by CRD according to IDALS designation. Due to annual crop planting patterns, the seasonal crop year was defined as April 1st – March 31st. Annual CRD application data were plotted with corresponding yearly SDWIS water contamination data including number of atrazine detections, percent of atrazine detections from all measurements, and mean annual atrazine concentrations. Mean

annual atrazine concentrations were calculated including field measurements that were below the LOD (censored data). Censored data was transformed by the substitution method of $LOD/\sqrt{2}$ (Hewitt and Ganser, 2007). The $LOD/\sqrt{2}$ substitution method was chosen due to the large size of the SDWIS dataset, its ease of implementation when examining mean exposures, as well as its reasonable accuracy in relation to other more robust, higher order methods, such as maximum likelihood estimations and log-probit regression analyses. Linear regression equations and coefficients of determination were examined for annual application trends by CRD. Simple linear regression was performed to evaluate trend lines from annual atrazine application amounts and annual mean atrazine concentrations.

Historical U.S. census data were used to evaluate segments of populations supplied by municipal and private well water sources. Water source of SDWIS measurements was examined for detection trends based on sampling time-of-year, detection frequency and range of detection concentrations.

SDWIS participating laboratories utilized EPA-approved analytical methods for the detection and quantification of study herbicides. For atrazine, des-ethylatrazine, and des-isopropylatrazine, methods 507 and 525.2 employed GC/nitrogen-phosphorous detection and capillary column GC/MS, respectively. For glyphosate, high performance liquid chromatography followed by post-column derivatization and fluorescence detection was used (method 547) (USEPA, 2012b).

As there were no detections for all glyphosate measurements, analyses primarily focused on regional SDWIS mean annual atrazine concentrations in comparison to annual IDALS CRD atrazine application estimates.

Results

Of the 12,133 SDWIS measurements available for this study covering the years 1990-2012, 8793 (72.5%) examined atrazine, 3132 (25.8%) examined glyphosate, and 208 (1.7%) examined finished municipal drinking water for atrazine metabolites des-ethyl and des-isopropyl atrazine (Table 2). All reported metabolite sampling and analyses were from the east central CRD. The southwest CRD had the highest average concentration (0.55 $\mu\text{g/L}$) for the years sampled whereas the south central CRD had the largest range of observed concentrations (0.1-10.1 $\mu\text{g/L}$).

Of the 8793 atrazine measurements, 2766 (31.5%) had detectable levels of atrazine equal to or greater than their respective method limit of detection (LOD), while only 7 (3.4%) of all metabolite measurements were detected at or above the LOD, and no detections were identified for the 3132 glyphosate measurements. There were eight reported LODs for atrazine ranging from 0.08 $\mu\text{g/L}$ – 1.3 $\mu\text{g/L}$. Of all atrazine measurements, 7227 (82.2%) had reported LODs of 0.1 $\mu\text{g/L}$, 1314 (14.9%) had no reported LOD, and 244 (2.8%) reported an LOD of 0.2 $\mu\text{g/L}$. All 208 metabolite measurements reported an LOD of 0.1 $\mu\text{g/L}$. Seven LODs were reported for the 3132 glyphosate measurements ranging from 1.0 $\mu\text{g/L}$ – 53.0 $\mu\text{g/L}$, of which 1527 (48.8%) reported a method LOD of 10.0 $\mu\text{g/L}$ and 1132 (36.1%) reported an LOD of 50.0 $\mu\text{g/L}$.

In order to further evaluate the primary source of contaminated drinking water, ground water, surface water, and ground water sources under the direct influence of surface water sources were grouped based on similar source (GW+GWP, GUP+GU, and SW+SWP). The number of detections and range of atrazine concentrations were determined for each group. Of the total 8793 atrazine measurements, 6988 (79.5%) were

sampled from drinking water taps supplied from ground water and purchased ground water systems (Table 3). An additional 1294 (14.7%) samples from drinking water were evaluated from surface water and purchased surface water sources. While more detectable measurements were observed from ground water sources (n=1617), those measurements comprised only 23.1% of the GW source samples. Nearly 70% of all surface water samples had detectable levels of atrazine with a markedly higher average concentration (0.97 $\mu\text{g/L}$) and a broader range of concentrations (0.1-10.1 $\mu\text{g/L}$) than ground water and purchased ground water under the direct influence of surface water (0.2, 0.1-1.9 $\mu\text{g/L}$) and ground water and purchased ground water (0.19, 0.1-5.0 $\mu\text{g/L}$).

The drinking water source for all seven metabolite detections were from ground water under the direct influence of surface water source(s). 88.7% of all glyphosate measurements were sampled from ground water sources (data not shown). A slightly smaller percentage (8.6%) of all glyphosate measurements were sampled from surface water sources as compared to all atrazine measurements (14.7%).

Annual statewide SDWIS atrazine concentration measurements were evaluated in comparison to IDALS atrazine application data for the years 1990-2004. Annual atrazine applications in millions of pounds increased overall while SDWIS atrazine measurement concentration data suggest lower detectable levels of the herbicide found in drinking water over the study period (Figure 2). Examination by all Iowa CRDs (Appendix A) suggests a similar trend in the south central CRD to that found in the statewide analysis with slightly increasing application rates coupled with lower detectable levels of atrazine over the study period (Figure 3).

Analysis of trend for amount of atrazine applied by year showed significant associations for four CRDs. The west central ($p=0.01$) and southeast ($p=0.049$) CRDs showed slight increase of pounds of atrazine applied over the study period and the north central ($p=0.005$) and northwest ($p=0.009$) CRDs showed slight decreases in atrazine use (Table 4). Trend analysis of SDWIS mean atrazine concentration data over the study period showed significant associations for four CRDs. The north central ($p=0.045$) showed an increase of mean atrazine concentration while the south central ($p=0.002$), southeast ($p=0.002$), and the east central ($p=0.01$) CRDs all showed decreased annual mean atrazine concentrations (Table 5).

Discussion

Historical herbicide contaminant data from Iowa's SDWIS does not suggest that municipal drinking water systems have persistent and elevated levels of atrazine, glyphosate, and atrazine breakdown products. However, the data suggests that drinking water in Iowa has been contaminated by atrazine in public water systems as evidenced by its detection in many finished, post-treatment drinking water supplies. Rarely was the EPA's recommended MCL of $3 \mu\text{g/L}$ exceeded: 21 measurements of 12,133 (0.17%) were $\geq 3 \mu\text{g/L}$ and 13 were from the south central CRD alone. The MCL of $700 \mu\text{g/L}$ set for glyphosate was never exceeded as evidenced by no observed detections ($\text{LOD} < 53 \mu\text{g/L}$).

There appears to be no correlation between atrazine usage trends and reported SDWIS finished drinking water measurements. As atrazine usage gradually increased over the study period, numbers of atrazine detections and annual atrazine mean concentrations decreased over the study period. Further examination of quarterly atrazine

measurements suggested that overall mean concentrations increased the six months (July – December) following the typical application time period of April/May (Table 6). The fate and transport of atrazine may partially explain this observation, particularly as it relates to atrazine's half-life in soil and water. The half-life for atrazine has been estimated to range from 13-261 days and 60-100 days in soil and water, respectively, and following high volume applications of the herbicide, it may persist in the environment for months at elevated concentrations. The relatively longer observed half-life in soil may make it available as a contaminant to adjacent water supplies through leaching and runoff. For instance, if a concentration of 10 µg/kg of atrazine is measured from soil and the half-life is estimated at 120 days, and environmental conditions are such that it minimizes degradation by sunlight and transport from the testing location, ~5 µg/kg would remain after 120 days. Following another 120 days (now at 240 days, or nearly eight months), and assuming similar environmental conditions, 2.5 µg/kg of the original 10 µg/kg of atrazine would remain, and so on. Other factors, such as environmental drift from post-emergent application events and residue transport by airborne dust particles during the fall harvest may contribute to increased detections and higher concentrations during this time period. Quarterly mean atrazine concentrations in surface water were more than three times those observed from ground water sources during the same time period (data not shown). The highest quarterly maximum concentrations were also found in surface water which may suggest multiple contamination mechanisms to Iowa's surface water sources.

While post-treatment drinking water is tested throughout Iowa, private well water systems are not required to test pesticide concentrations, yet many of these water sources

are susceptible to pesticide contamination (Kross *et al.*, 1990). Although private wells are supplied by ground water sources, it has been shown that drinking water derived from these sources may have the least contamination. Other factors may contribute to the pesticide contamination potential to private wells, such as being under the direct influence of nearby contaminated surface waters or proximity to farms and farm fields where these chemicals are being mixed and applied. It has been estimated that over 206,000 Iowans (6.8%) are on private well water systems and yet there is very little data available demonstrating pesticide contaminant profiles (IDNR, 2010).

From April, 1988 through June, 1989, the Iowa State-Wide Rural Well-Water Survey (SWRL) was conducted. A joint research effort by IDNR and the University of Iowa Center for Health Effects of Environmental Contaminants (CHEEC), SWRL evaluated 686 private well water sites located across all 99 Iowa counties (Kross *et al.*, 1990). Included in the contaminant analyses were 27 pesticides and 5 pesticide breakdown products, though glyphosate was not analyzed. Atrazine and its metabolites were detected in approximately 8% of wells sampled in the study area, though not in concentrations that exceeded the EPA's atrazine MCL of 3 $\mu\text{g/L}$. Results from this study further suggest that depth and well location in relation to pesticide mixing and application events are key components in the probability of a well being contaminated by atrazine and other pesticides and chemicals. Shallow wells (<100 feet), which are typically large diameter seepage wells had the highest proportion of contaminants, while deeper, drilled cement-cased wells had little contamination. The south central, southwest, and northwest CRDs showed the greatest proportion of contaminated wells where nearly 75% have

depths of <100 feet. It was estimated that half of Iowa's wells meet this criterion, and 64% of total atrazine and pesticide detections were from wells <100 feet.

This study was unable to demonstrate an association between quantity of atrazine and glyphosate applied in Iowa and concentrations of these herbicides detected in municipal drinking water systems. The SDWIS data did not show elevated levels of atrazine, its metabolites, and glyphosate, particularly when compared to the EPA's regulated MCLs. However, there is evidence to suggest that atrazine is environmentally persistent and may contaminate municipal drinking water systems. The SDWIS data also showed regional differences between the nine CRDs in number of detections and mean concentrations, as well as temporal differences based on quarterly estimates and evaluation of drinking water source (ground water vs surface water). Future pesticide exposure assessment studies in Iowa would more effectively examine potential risk to a broader segment of rural populations if they were to include sampling from private well water sources. Increased periodic testing from both private and public water supplies may also help to create more accurate contamination profiles. Also, environmental pesticide monitoring in and around rural homes will contribute further in the evaluation of alternate exposure pathways and estimates of absorbed dose should be included with biomonitoring efforts within study populations.

Conclusion

This study examined herbicide contaminant data from a statewide monitoring program covering 15 years and the relationship of mean contaminant levels to application intensities throughout Iowa's nine crop reporting districts. As pesticide usage trends in Iowa and throughout agriculture-based regions continue to demonstrate increased annual

herbicide applications, particularly glyphosate and glyphosate-based herbicides, continued surveillance of their persistence in and impact to the environment as well as potential harm to human health is vital.

While future studies continue to provide evidence of the potential health effects associated with exposure to atrazine and glyphosate, the development and execution of more robust research studies examining multiple pesticide exposure pathways is required for more precise and accurate assessments of potential risk to susceptible populations.

As glyphosate use continues to rise each year, it seems likely that data generated from agrichemical surveillance programs would indicate an environmental presence of the herbicide in raw and finished water supplies. With the exception of the east central CRD, Iowa's SDWIS dataset indicates that monitoring efforts for glyphosate ceased in 1997 while application rates for the herbicide have nearly doubled, suggesting that state-wide sampling and analysis for glyphosate should be reintroduced. Improved detection and quantification methods are needed for more sensitive pesticide contaminant analyses of both public and private water systems, particularly those more highly-susceptible water sources. Inclusion of an analytical method's limit of quantification (LOQ) in addition to its LOD would provide for a higher degree of confidence in reported laboratory results. More periodic testing of water systems, both raw and finished drinking water, may help to establish more reliable contamination profiles adding to an essential increased understanding of pesticide contaminant fate and transport properties through soil and water matrices.

Many commercial pesticide formulations incorporate other ingredients in combination with the active ingredient, such as adjuvants and surfactants, in order to

increase the performance and effectiveness of the agrichemical. Future herbicide exposure assessment studies should consider this when evaluating potential routes of exposure and health outcomes.

Future environmental herbicide contamination studies may consider inclusion of pre- and post-treatment sampling in examining public drinking water systems as well as increased sampling and analyses from private well water and surface water sources. As more and more people rely on bottled water, an evaluation of commercially available drinking water may potentially indicate an additional source of exposure to agrichemicals.

Continued analysis of the SDWIS database may help future researchers identify areas of concern with regards to herbicide contaminated drinking water as a potential pathway of exposure as well as guide them in their determination of sampling frequencies. While annual atrazine applications have leveled off, it remains the second leading herbicide used for agriculture in Iowa behind glyphosate. Considering the ever-increasing amounts of glyphosate-based herbicides being applied to Iowa's farm fields each year, improved monitoring may begin to show glyphosate detections not only in unfinished ground and surface water supplies, but public and private drinking water systems as well.

Figure 2: State-wide Iowa SDWIS measurements and annual atrazine usage, 1990-2004.
LOD = 0.1 μ g/L

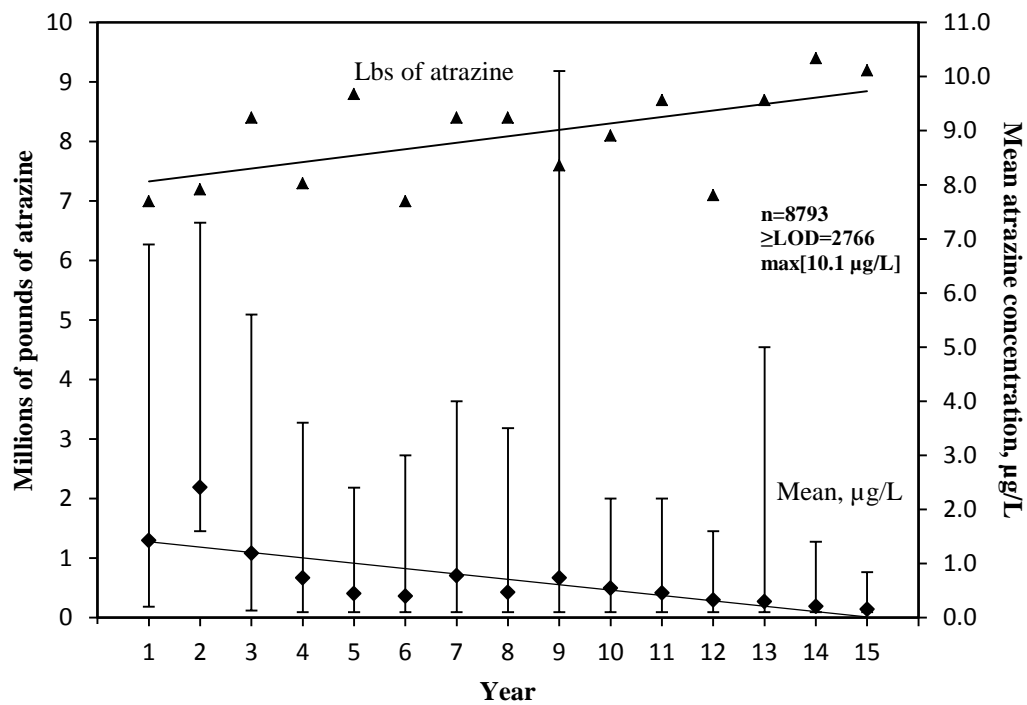


Figure 3: Iowa south central CRD SDWIS measurements and annual atrazine usage, 1990-2004. LOD = $0.1\mu\text{g/L}$

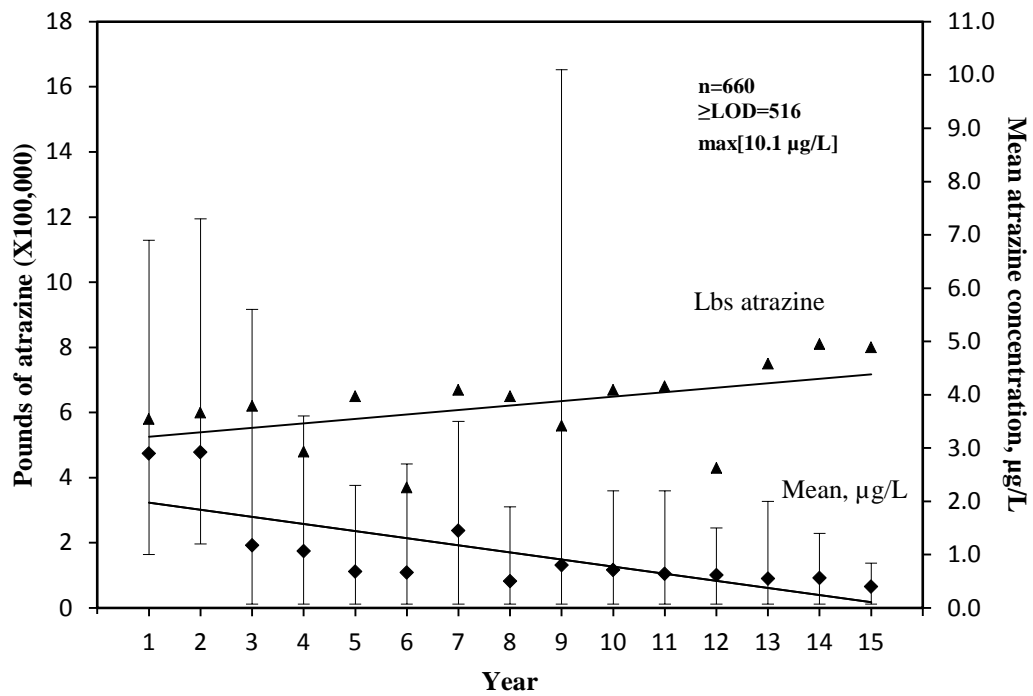


Table 1: Atrazine exposure pathways studies

Pathway Source	Study location and population	Measurement	Reference
Air Indoor	Urban residences of non-occupationally exposed adults in FL and MA	24-hour continuous fixed sample in high-traffic locations	Whitmore et al, 1994
Air Indoor	Non-urban residences with domestic pesticide use in NC; ≥ 1 child aged 6-months to 5-years	Two 24-hour continuous, fixed samples at differing heights (breathing zones)	Lewis et al, 1994
Air Indoor	Urban and non-urban MN households with children aged 3-12	Environmental concentrations by integrated indoor air sample	Quackenboss et al, 2000 and Pellizzari et al, 2003
Air Indoor	20 unexposed and 21 occupationally-exposed adults (veterinarians, florists, and gardeners)	24-hour aerosol and particulate air sampling in residences and places of occupation	Bouvier et al, 2006
Air Outdoor	Urban residences of non-occupationally exposed adults in FL and MA	24-hour continuous fixed sample in frequently used locations	Whitmore et al, 1994
Air Outdoor	Urban and non-urban MN households with children aged 3-12	Environmental concentrations by integrated outdoor air sample	Quackenboss et al, 2000 and Pellizzari et al, 2003
Air Personal	Urban residences of non-occupationally exposed adults in FL and MA	24-hour continuous personal sampler on or in close proximity to study participant	Whitmore et al, 1994
Air Personal	Urban and non-urban MN households with children aged 3-12	Personal air sample concentrations from primary breathing zone	Quackenboss et al, 2000 and Pellizzari et al, 2003
Soil	Non-urban residences with domestic pesticide use in NC; ≥ 1 child aged 6-months to 5-years	Sampled from doormat at most frequently used doorway and primary play/walkways for child(ren)	Lewis et al, 1994
Soil	Experimental agricultural test field	Dissipation measurements of atrazine and breakdown products under field conditions examining soil and soil-water samples	Tasli et al, 1996
Soil	Urban and non-urban MN households with children aged 3-12	Composite surface soil sample concentrations from primary outdoor activity areas	Quackenboss et al, 2000 and Pellizzari et al, 2003
Water	Experimental agricultural test field	Concentration measurements of tile-drained water from corn cultivated test fields	Muir and Baker, 1976
Drinking Water	Urban and non-urban MN households with children aged 3-12	Tap or bottled water concentrations from each household	Quackenboss et al, 2000 and Pellizzari et al, 2003

Table 1 continued

Pathway Source	Study location and population	Measurement	Reference
Surface Dust Indoor	Urban and non-urban MN households with children aged 3-12	Surface wipe samples from primary indoor activity areas	Quackenboss et al, 2000 and Pellizzari et al, 2003
Carpet Dust Indoor	Non-urban NC residences with domestic pesticide use; ≥ 1 child aged 6-months to 5-years	Vacuum collection and hand presses at 3 locations: high-traffic, area frequented by child, low-traffic	Lewis et al, 1994
Carpet Dust Indoor	Urban and non-urban MN households with children aged 3-12	Vacuumed dust samples from selected high-traffic areas	Quackenboss et al, 2000 and Pellizzari et al, 2003
Diet	Urban and non-urban MN households with children aged 3-12	Duplicate composite food and beverage samples for all consumed meals	Quackenboss et al, 2000 and Pellizzari et al, 2003

Table 2: Iowa SDWIS summary statistics by crop reporting district, 1990-2012

Crop Reporting District and active ingredient (A.I.)	Years	Total measurements	Detectable measurements (% of total)	A.I. concentration, µg/L	
				Mean	Range
Central					
Atrazine	1993-2012	864	190 (22)	0.29	0.1-3.5
Glyphosate	1993-1997	400	0		
Metabolites ^a	NR ^b	0	0		
East Central					
Atrazine	1990-2012	2439	726 (29.8)	0.22	0.1-3.7
Glyphosate	1993-2010	844	0		
Metabolites	2007-2012	208	7 (3.4)	0.13	0.1-0.16
North Central					
Atrazine	1993-2011	607	137 (22.6)	0.12	0.1-0.48
Glyphosate	1993-1996	253	0		
Metabolites	NR	0	0		
Northeast					
Atrazine	1993-2012	1642	347 (21.1)	0.16	0.1-1.1
Glyphosate	1993-1997	588	0		
Metabolites	NR	0	0		
Northwest					
Atrazine	1993-2012	756	302 (39.9)	0.21	0.1-2.4
Glyphosate	1993-1997	247	0		
Metabolites	NR	0	0		
South Central					
Atrazine	1993-2012	660	516 (78.2)	0.22	0.1-10.1
Glyphosate	1993-1997	101	0		
Metabolites	NR	0	0		
Southeast					
Atrazine	1990-2012	587	219 (37.3)	0.4	0.1-3.3
Glyphosate	1993-1997	180	0		
Metabolites	NR	0	0		
Southwest					
Atrazine	1993-2012	518	157 (30.3)	0.55	0.1-4.0
Glyphosate	1993-1997	198	0		
Metabolites	NR	0	0		
West Central					
Atrazine	1993-2012	720	172 (23.9)	0.21	0.1-5.0
Glyphosate	1993-1997	321	0		
Metabolites	NR	0	0		
Total		12133			

^aMetabolites include des-ethylatrazine and des-isopropylatrazine

^bNot Reported

Table 3: Iowa SDWIS atrazine measurements by drinking water source, 1990-2012

Drinking water source	Total atrazine measurements	Detectable measurements (% of total)	Atrazine Concentration, $\mu\text{g/L}$	
			Mean	Range
GUP + GU ^a	511	251 (49.1)	0.2	0.1-1.9
GW + GWP ^b	6988	1617 (23.1)	0.19	0.1-5.0
SW + SWP ^c	1294	898 (69.4)	0.97	0.1-10.1

^a Ground water and purchased ground water under the direct influence of surface water

^b Ground water and purchased ground water

^c Surface water and purchased surface water

Table 4: Linear regression of atrazine application as a function of year, 1990-2004

CRD ^a	R ²	p ^b	95% Confidence Interval of R ²	
			Lower	Upper
Central	0.28	0.08	-0.02	0.34
East central	0.11	0.24	-0.31	0.09
North central	0.57	0.005	0.06	0.27
Northeast	0.10	0.33	-0.33	0.12
Northwest	0.51	0.009	-0.23	-0.04
South central	0.24	0.06	-0.01	0.28
Southeast	0.27	0.049	0.001	0.39
Southwest	0.22	0.12	-0.04	0.32
West central	0.51	0.01	0.05	0.28

^aIowa crop reporting district

^bProbability that the slope of atrazine application is zero with significance level $\alpha=0.05$

Table 5: Linear regression of atrazine concentration as a function of year, 1990-2004

CRD ^a	R ²	p ^b	95% Confidence interval of R ²	
			Lower	Upper
Central	0.01	0.71	-0.03	0.02
East central	0.39	0.01	-0.05	-0.01
North central	0.34	0.045	0.0001	0.01
Northeast	0.05	0.47	-0.004	0.01
Northwest	0.02	0.69	-0.01	0.01
South central	0.54	0.002	-0.21	-0.06
Southeast	0.54	0.002	-0.05	-0.01
Southwest	0.02	0.70	-0.04	0.05
West central	0.12	0.28	-0.004	0.01

^aIowa crop reporting district

^bProbability that the slope of atrazine concentration = zero with significance level $\alpha=0.05$

Table 6: Iowa SDWIS quarterly atrazine measurements, 1990-2012

Reported time period	Atrazine Measurements	Mean (µg/L)	Minimum concentration (µg/L)	Maximum concentration (µg/L)	Number of measurements ≥ 1 µg/L	Number of measurements ≥ 3 µg/L ^b
January – March	2277	0.11	< LOD ^a	6.9	79	3
April – June	2357	0.11	< LOD	10.1	70	7
July - September	2187	0.15	< LOD	7.3	94	7
October - December	1972	0.19	< LOD	4.9	77	4
Total	8793	0.13	< LOD	10.1	320	21

^a < LOD indicates no detection below atrazine concentration of 0.2 µg/L

^bEPA's Maximum contaminant level (MCL) for atrazine

CHAPTER III

CONCLUSION

This study examined herbicide contaminated drinking water from Iowa's Safe Drinking Water Information System. Analysis of SDWIS measurements suggest similar atrazine concentration ranges reported from other monitoring studies throughout the U.S. (Quackenboss *et al.*, 2000). All measurements were sampled from municipal drinking water systems across the state and do not represent the potential burden to private well water sources due to herbicide contamination. As such it is difficult to estimate potential exposures in susceptible populations.

In 2010, in effort to evaluate atrazine and glyphosate non-occupational exposures in rural Iowa communities, a pilot study initially funded by the University of Iowa's Environmental Health Sciences Research Center (EHSRC) and later the Heartland Center for Occupational Health and Safety, recruited, enrolled and followed 64 adults from 33 Iowa households located across 3 counties. Biologic and drinking water sampling was performed at two separate time periods over the course of 8 months (July/August and February/March). While results from sample analyses are pending, a retrospective look at the study's design has revealed issues which may have been improved upon during the sampling time frame. Had the resources been available, additional sampling and sampling from households served by private well water sources would have strengthened the study's assessment of potential herbicide exposures. Municipal drinking water from ground water sources principally served the study population with the exception of four households, all of which were served by private well supplied from ground water. Utilization of the state-wide SDWIS database may have helped to identify regions (e.g.

counties) with more defined pesticide contaminant concentration levels for comparison. Specifically, inclusion of drinking water sampling from households within the south central CRD may have yielded higher annual and quarterly mean concentrations than what was observed in the three pilot study counties, all of which were from the east central CRD. Specific municipalities may also have been targeted due to historical SDWIS data. Following more comprehensive exposure assessment studies which have incorporated additional environmental monitoring activities, such as air and dust sampling in order to assess alternate exposure pathways would have been warranted.

Data generated by SDWIS may prove to be useful in demonstrating differences in drinking water herbicide contaminant concentrations at regional as well as municipal levels. Utilization of SDWIS data may serve as a viable indicator for identifying areas of concern and susceptible populations when designing future herbicide exposure assessment studies. It may also be useful to integrate other agrichemical usage estimates, such as those generated from NASS, EPA, state, and local government surveillance programs, in these evaluations.

The field of industrial hygiene can play a critical role in developing and advancing the scientific methods required for effective environmental pesticide contaminant monitoring studies as well as eventual assessments of exposure and risk. Industrial hygiene utilizes many sampling tools and analytical methods for a variety of biologic and environmental matrices to examine the source and presence of pesticide contaminants as well as to evaluate dose estimations. Many of the sampling and analysis techniques available to the industrial hygienist to be employed in occupational settings can be equally as effective in environmental pesticide contaminant surveillance and

exposure assessments, such as indoor air quality analyses, examination of surface wipes and dust samples, evaluation of drinking water and food samples, and biomonitoring efforts.

Historically, pesticide exposure studies have typically been based on occupational exposures experienced by those workers who mix and apply pesticides, such as the farmer or commercial applicator. Pathways and routes of exposure may be more defined in such studies; for instance, inhalation from airborne mists generated by spray applications or dermal absorption of the pesticide as a result of handling and mixing events. Exposure and resultant dose estimations may then be more easily quantitated. In assessing potential exposures due to environmental contaminants, however, the investigator may need to incorporate a variety of sampling strategies in order to evaluate all potential sources of exposure and, most likely, at concentrations much lower than those found in occupational settings.

Similar to studies examining pesticide exposures in households with family members who have occupational exposures, larger more comprehensive environmental contaminant monitoring and exposure studies may include assessments of occupational exposures experienced by individuals who work and live within the same study populations potentially increasing the range of observed exposure estimates. A broader range of exposures may also be observed from incorporating sampling strategies designed to capture environmental exposures before, during, and after pesticide application events in order to more effectively examine associations between exposure and adverse health outcomes.

APPENDIX

SCATTER PLOTS

Appendix contains additional scatterplots depicting herbicide usage trends and SDWIS concentration estimates for atrazine and glyphosate. U.S. glyphosate and atrazine estimates are plotted in millions of pounds. Annual SDWIS atrazine concentration levels are shown with IDALS atrazine use data by Iowa CRD. SDWIS data is plotted by percent of detections from annual measurements and mean atrazine concentrations while IDALS atrazine use data is plotted by hundreds of thousands of pounds.

Figure A1: Herbicide use, U.S. agricultural market sector, 2001-2007 estimates

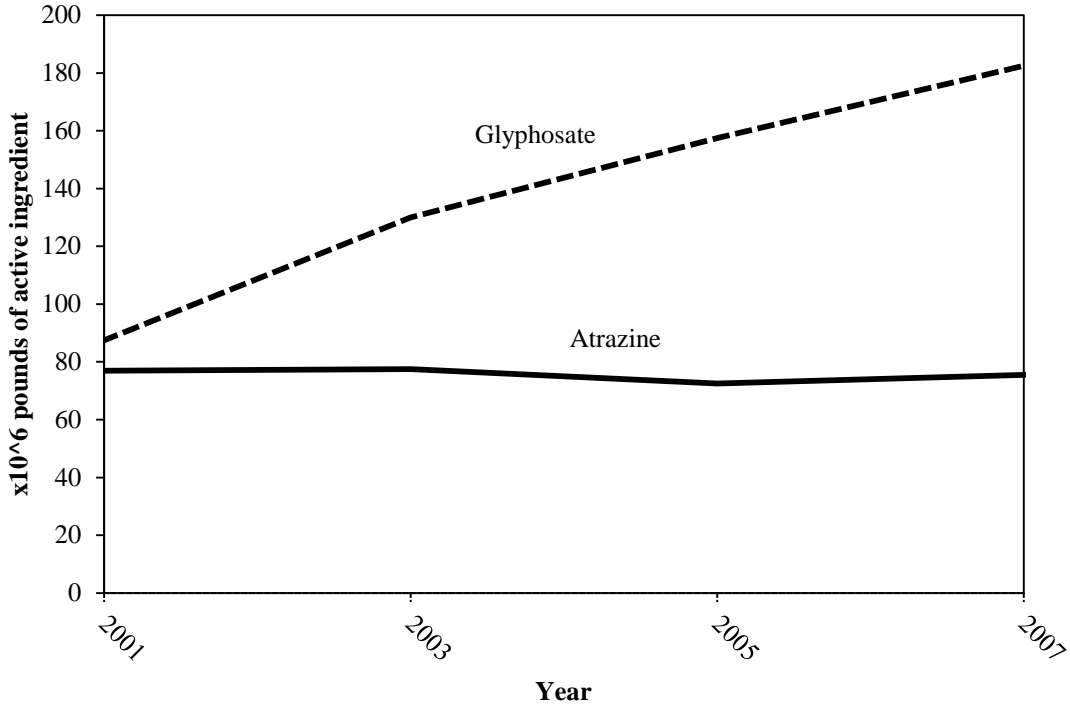


Figure A2: Central Iowa CRD, atrazine usage and percent detected

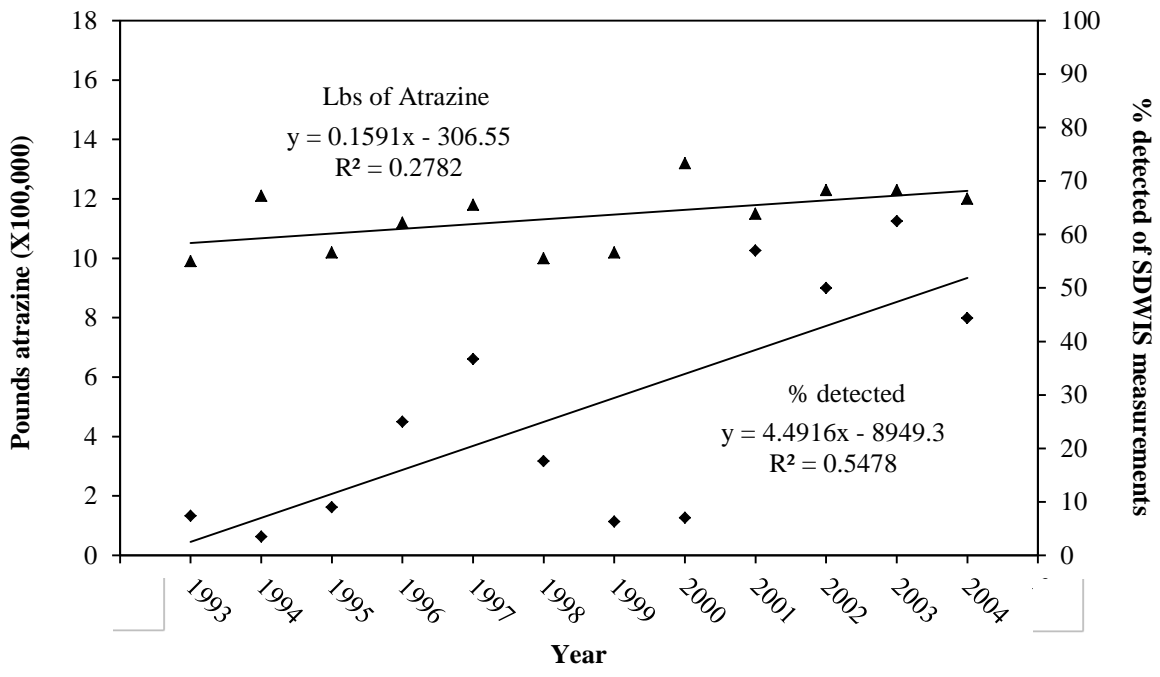


Figure A3: Central Iowa CRD, atrazine usage and concentration measurements

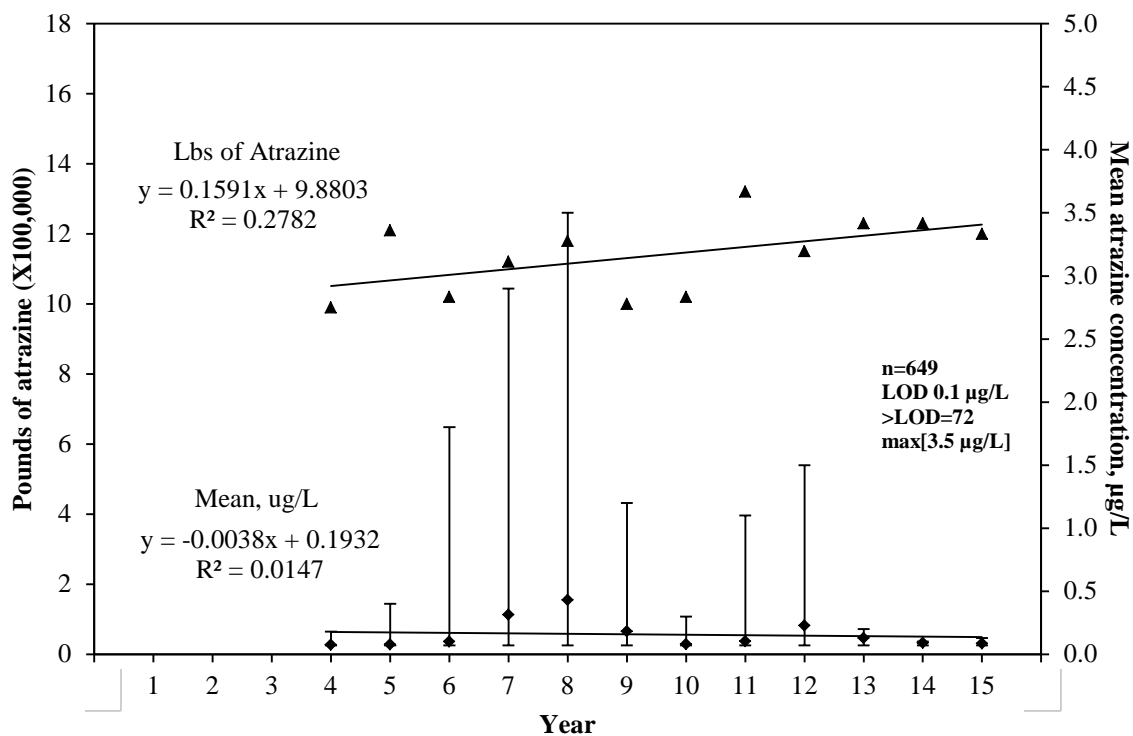


Figure A4: East Central Iowa CRD, atrazine usage and percent detected

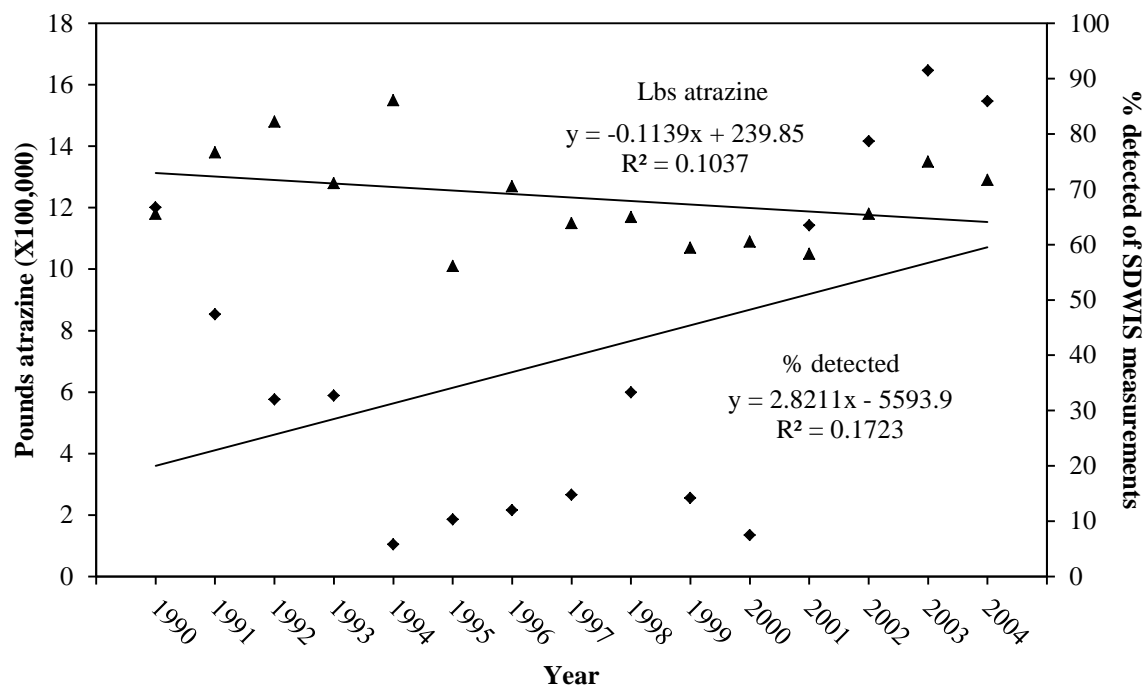


Figure A5: East Central Iowa CRD, atrazine usage and concentration measurements

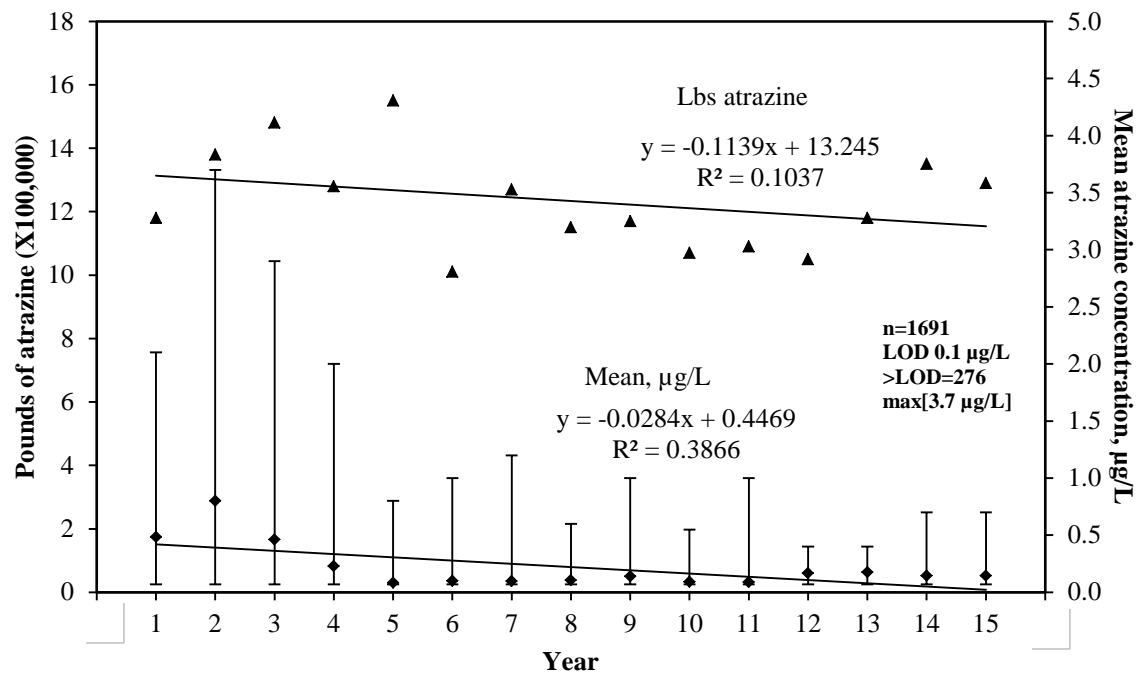


Figure A6: North Central Iowa CRD, atrazine usage and percent detected

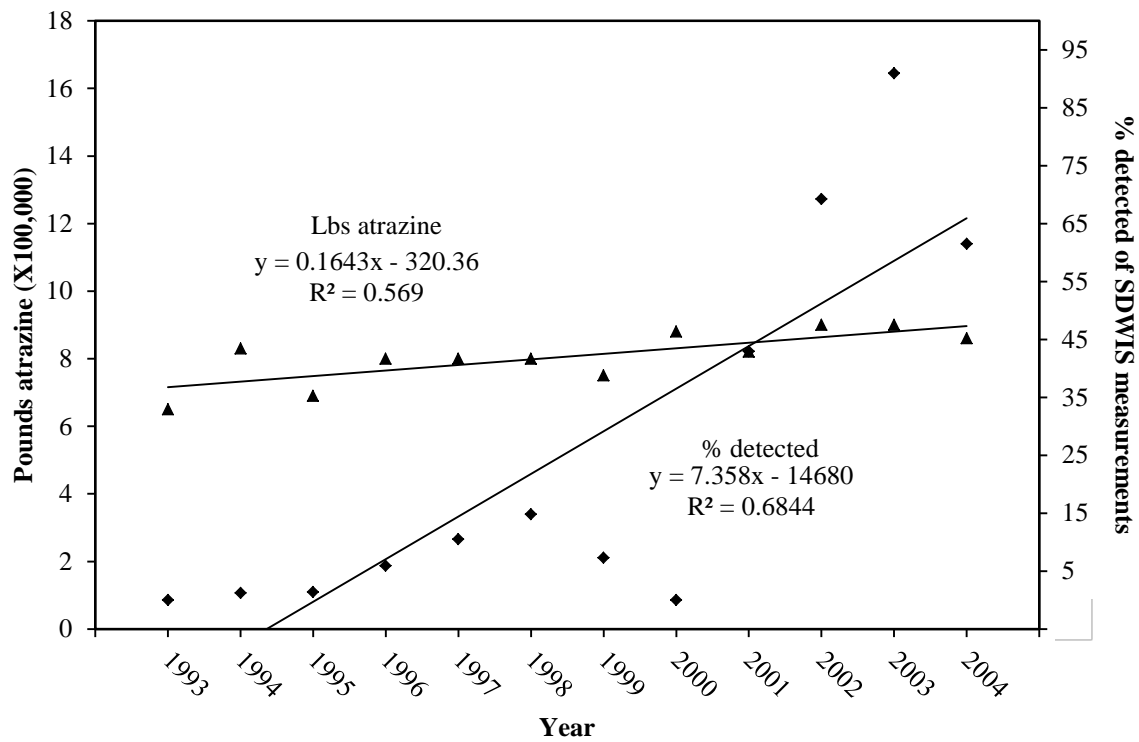


Figure A7: North Central Iowa CRD, atrazine usage and concentration measurements

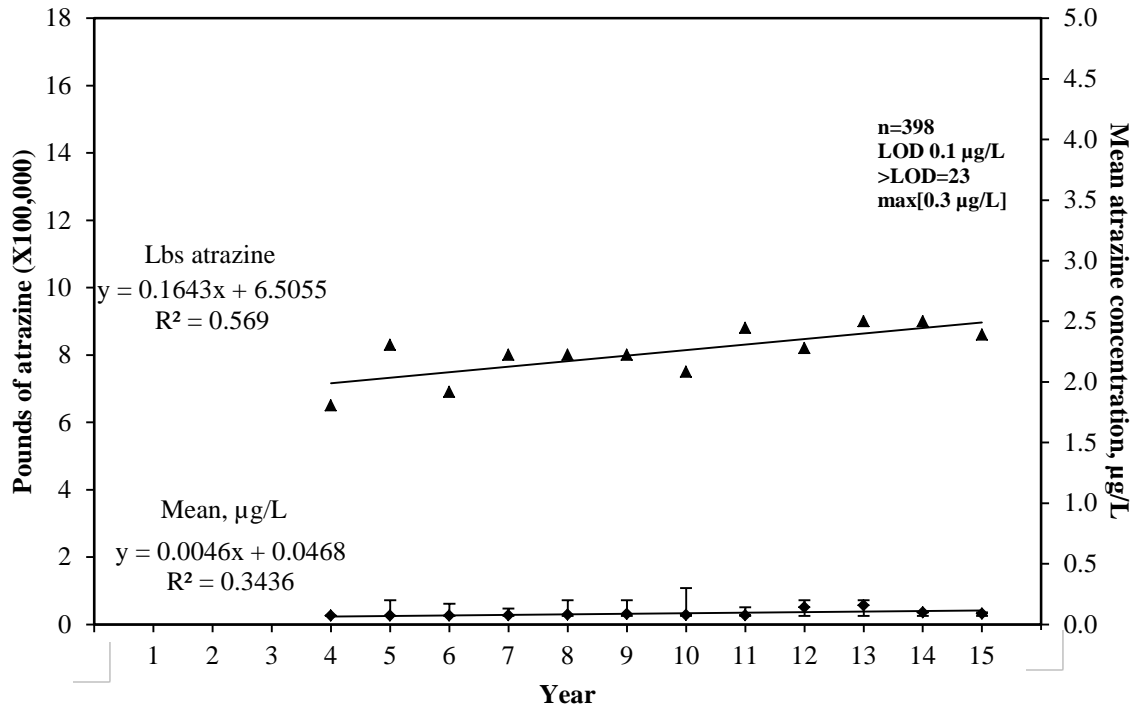


Figure A8: Northeast Iowa CRD, atrazine usage and percent detected

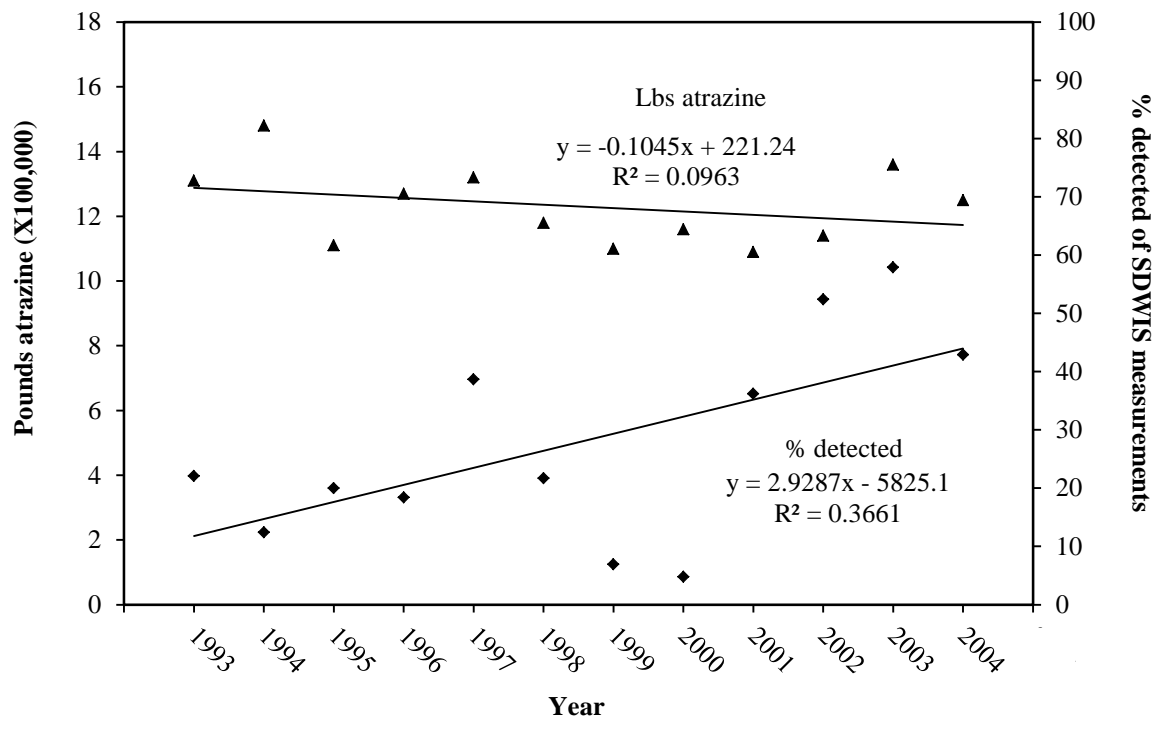


Figure A9: Northeast Iowa CRD, atrazine usage and concentration measurements

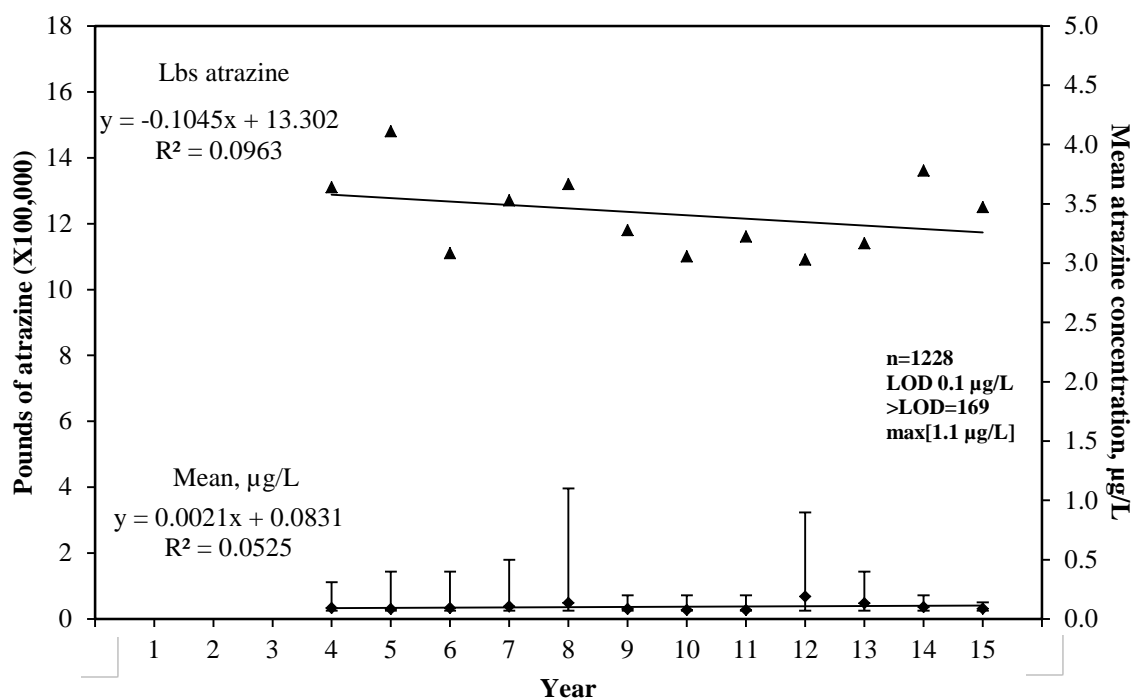


Figure A10: Northwest Iowa CRD, atrazine usage and percent detected

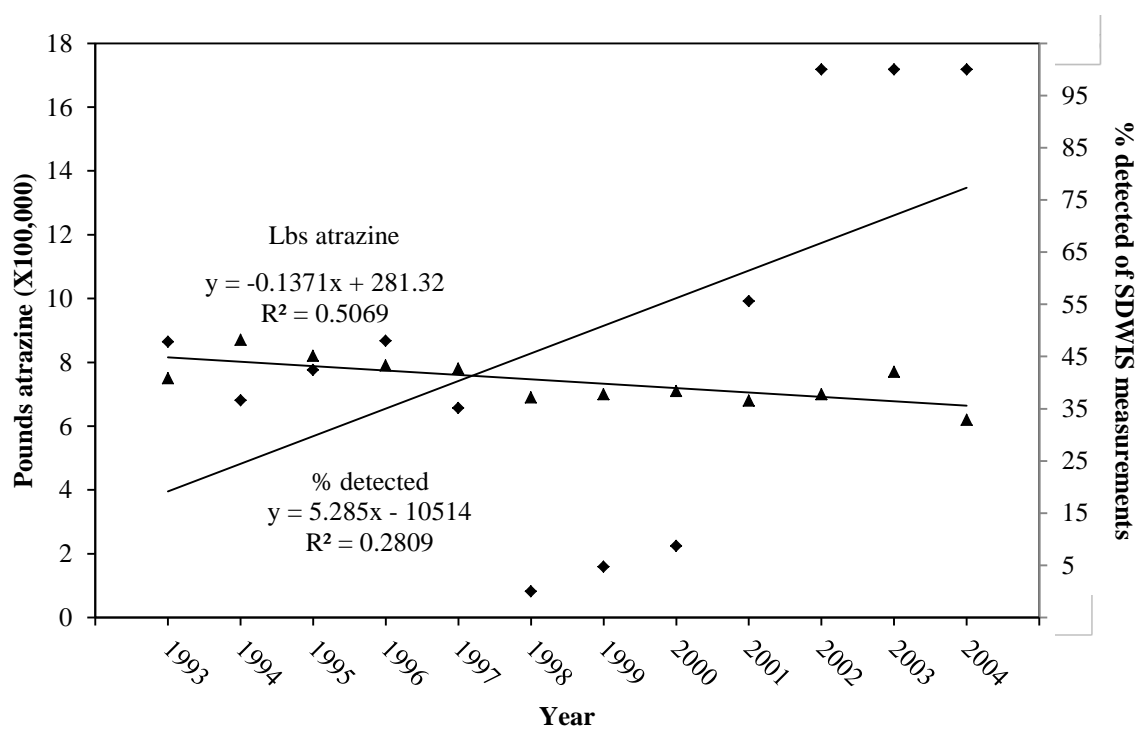


Figure A11: Northwest Iowa CRD, atrazine usage and concentration measurements

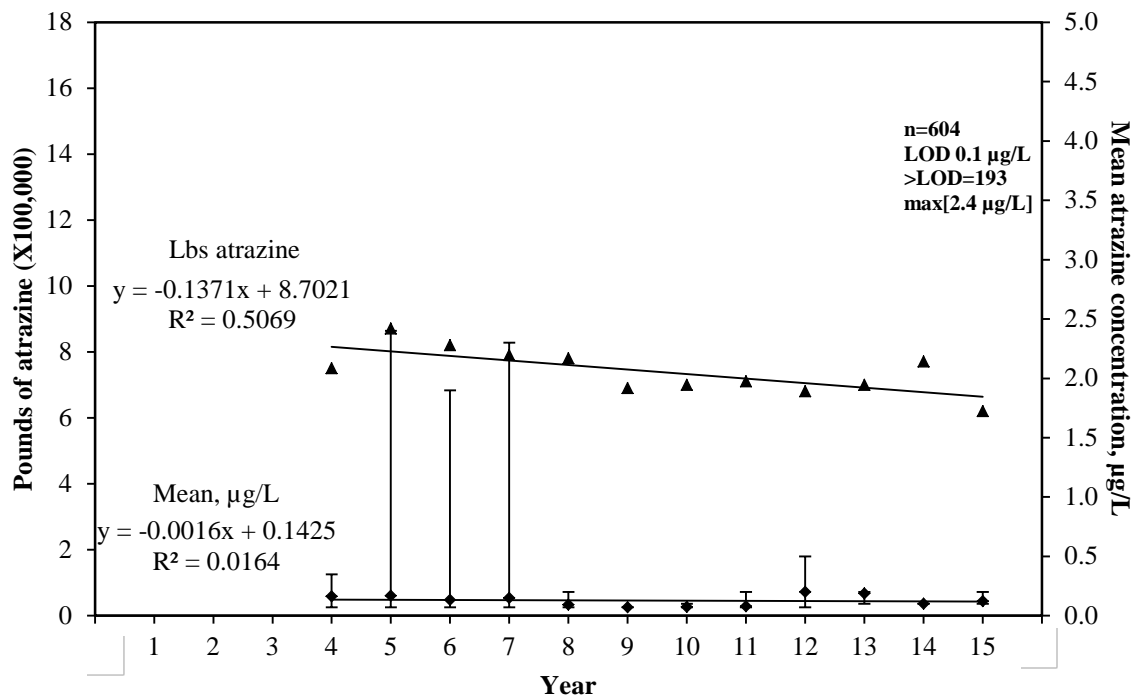


Figure A12: South Central Iowa CRD, atrazine usage and percent detected

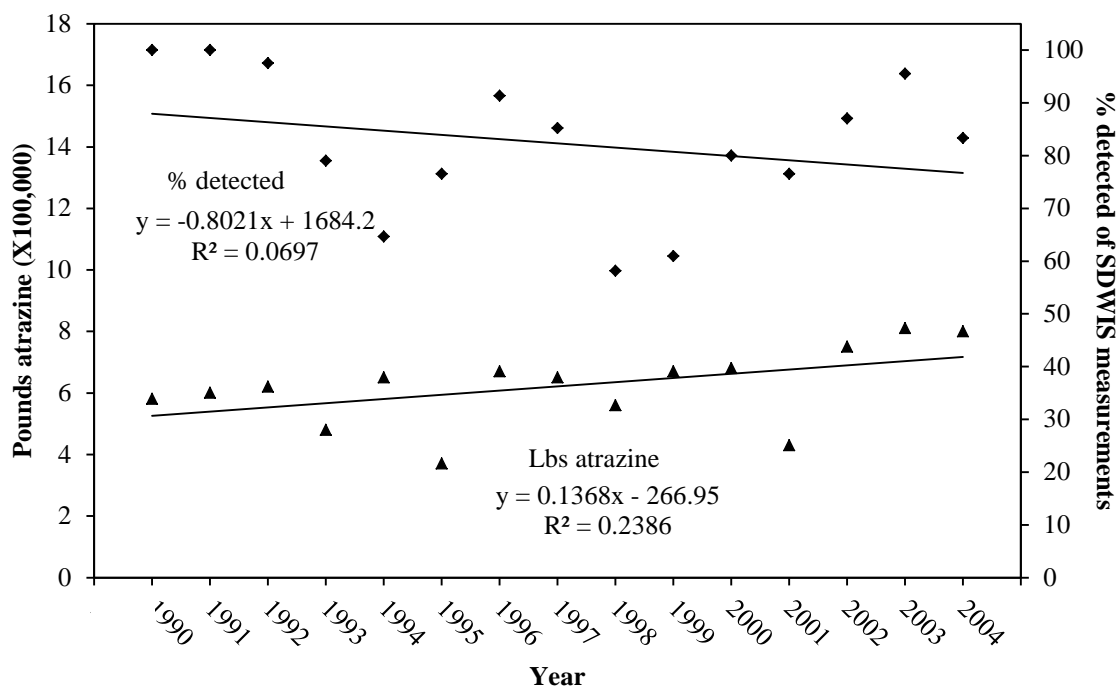


Figure A13: Southeast Iowa CRD, atrazine usage and percent detected

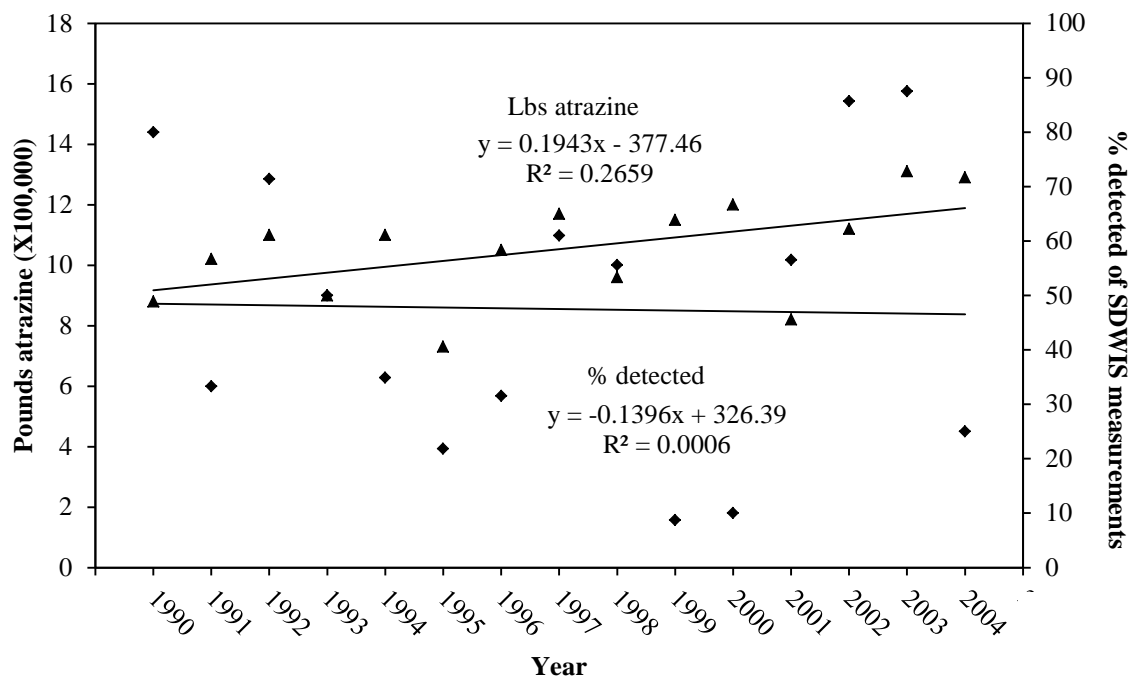


Figure A14: Southeast Iowa CRD, atrazine usage and concentration measurements

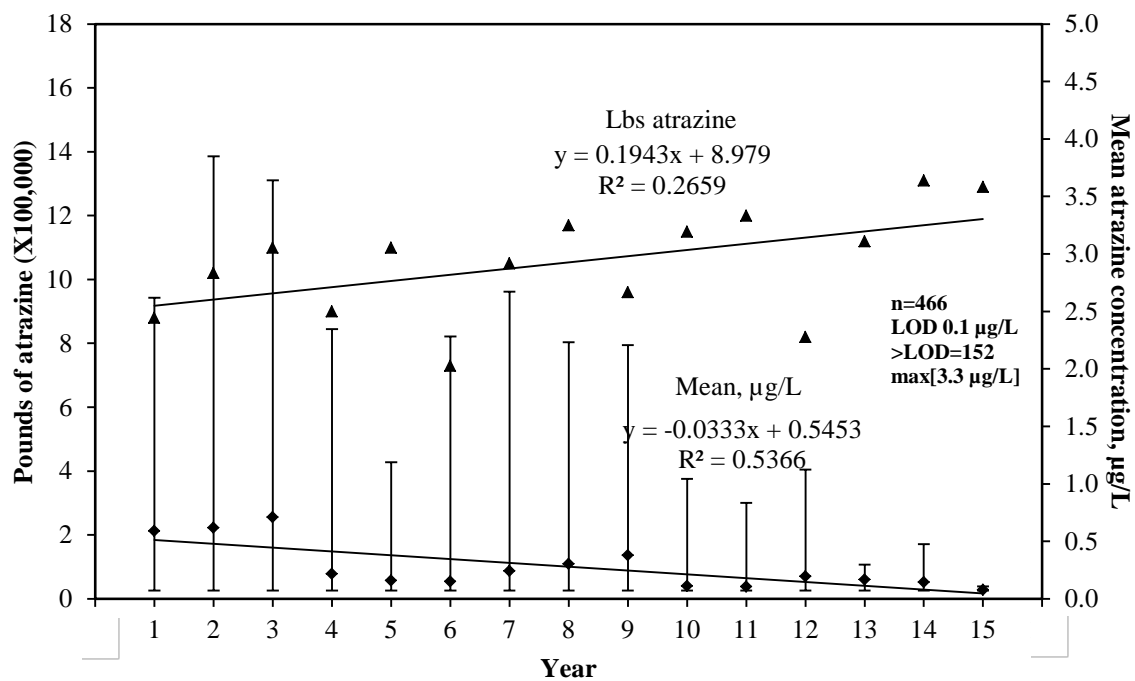


Figure A15: Southwest Iowa CRD, atrazine usage and percent detected

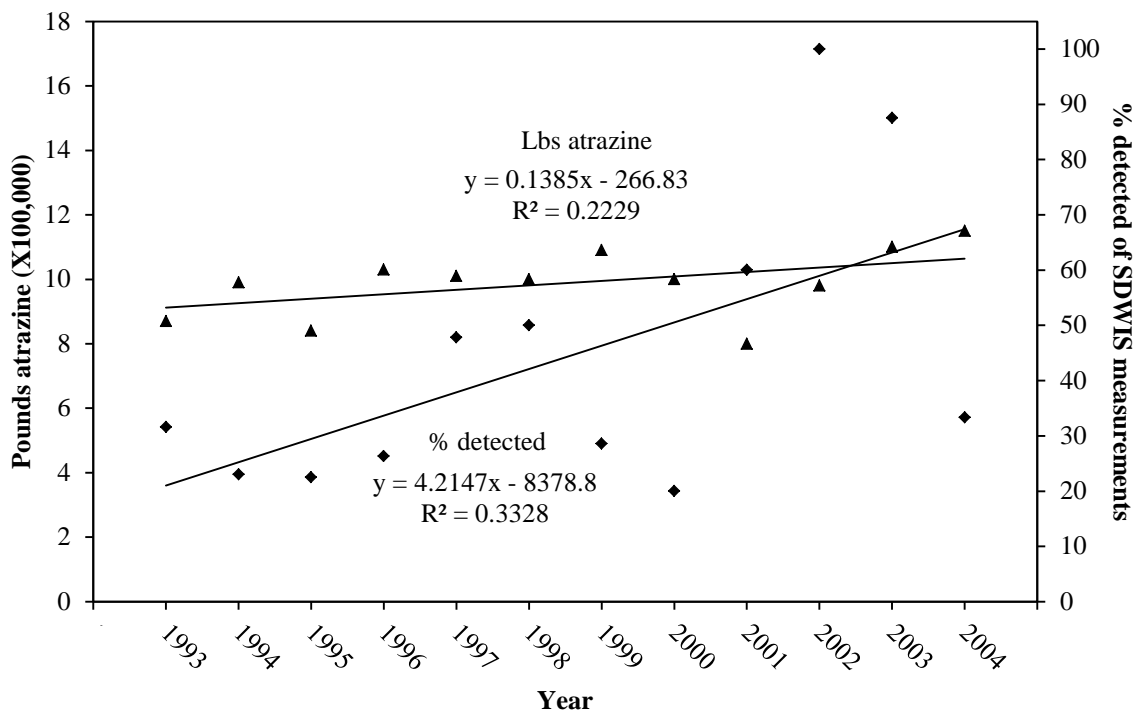


Figure A16: Southwest Iowa CRD, atrazine usage and concentration measurements

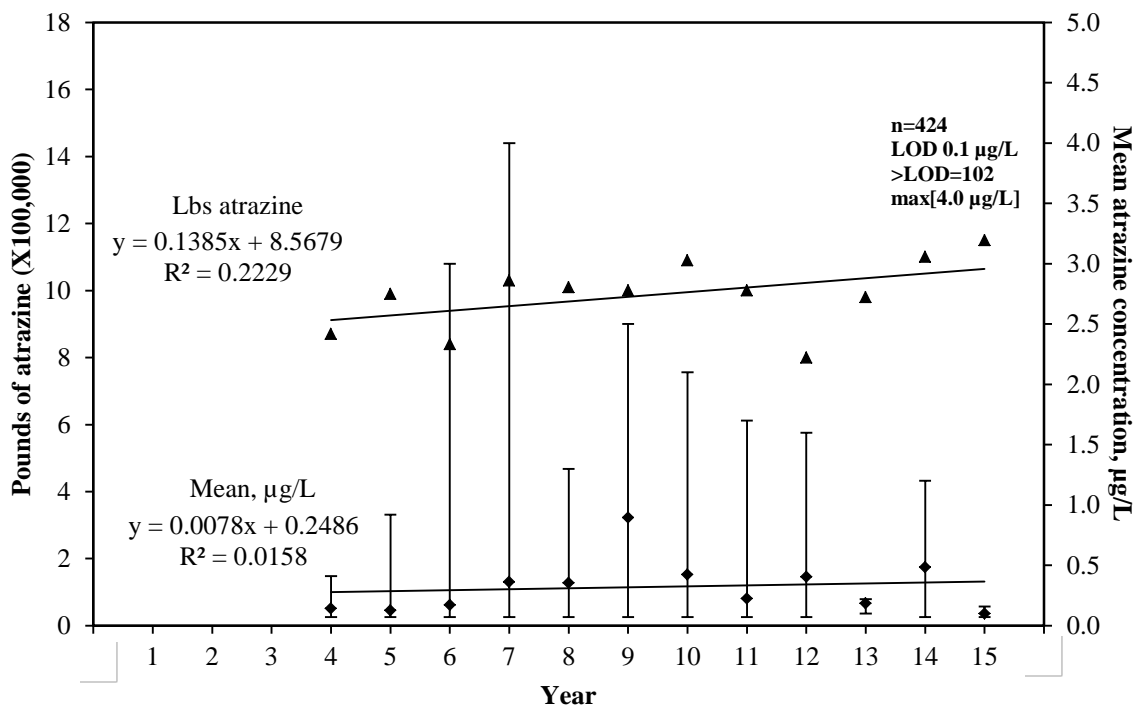


Figure A17: West Central Iowa CRD, atrazine usage and percent detected

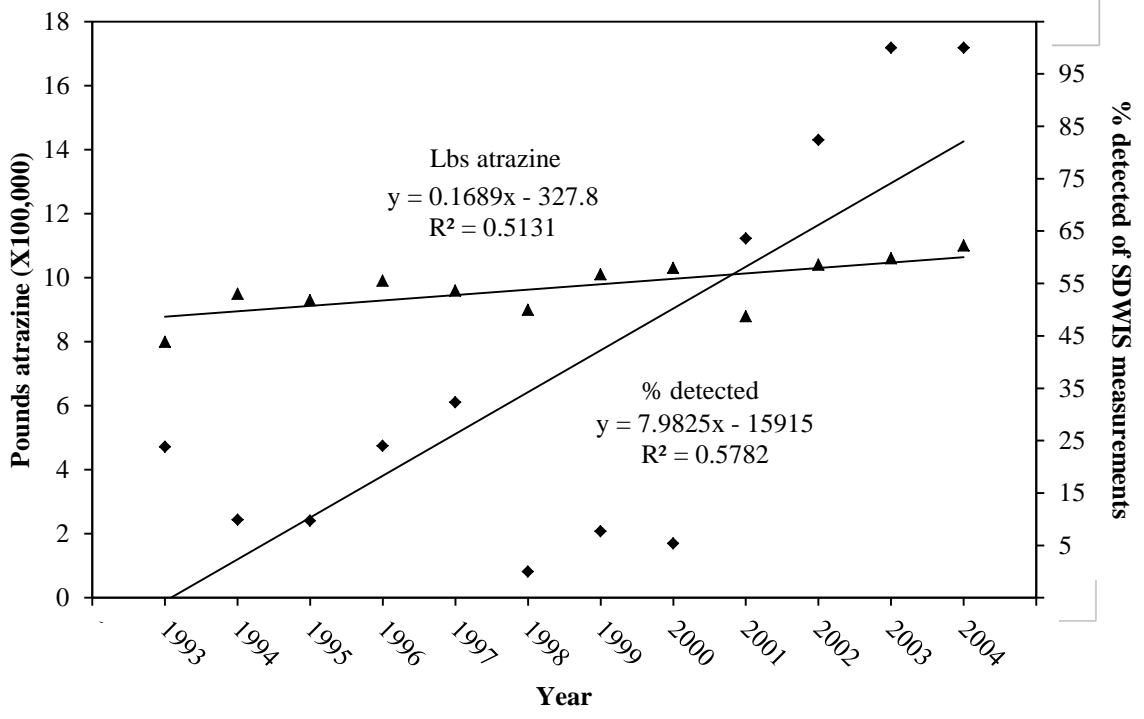
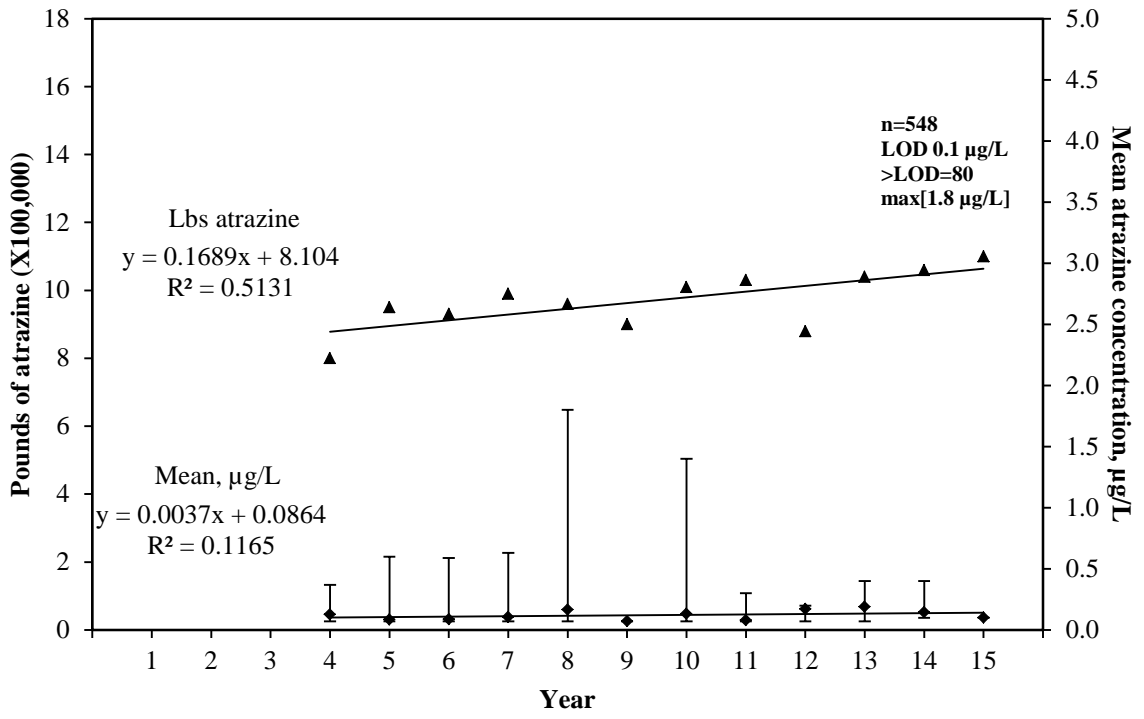


Figure A18: West Central Iowa CRD, atrazine usage and concentration measurements



REFERENCES

- Arbuckle, T. E., Zhiqiu, L., & Mery, L. S. (2001). An Exploratory Analysis of the Effect of Pesticide Exposure on the Risk of Spontaneous Abortion of an Ontario Farm Population. *Environmental Health Perspectives*, 109(8), 851-857.
- Baronti, C., Curini, R., D'Ascenzo, G., Di Corcia, A., Gentili, A., & Samperi, R. (2000). Monitoring Natural and Synthetic Estrogens at Activated Sludge Sewage Treatment Plants and in a Receiving River Water. *Environmental Science and Technology*, 34(24), 5059-5066.
- Barr, D. B. (2008). Biomonitoring of exposure to pesticides. *Journal of Chemical Health and Safety*, 15(6), 20-29.
- Battaglin, W., Kolpin, D., Scribner, E., Kuivila, K., & Sandstrom, M. (2005). Glyphosate, other herbicides, and transformation products in midwestern streams, 2002. *Journal of the American Water Resources Association*, 41(2), 323-332.
- Bell, E. M., Hertz-Picciotto, I., & Beaumont, J. J. (2001). A case-control study of pesticides and fetal death due to congenital anomalies. *Epidemiology*, 12(2), 148-156.
- Benachour, N., Sipahutar, H., Moslemi, S., Gasnier, C., Travert, C., & Seralini, G. E. (2007). Time- and dose-dependent effects of roundup on human embryonic and placental cells. *Archives of Environmental Contamination and Toxicology*, 53(1), 126-133.
- Biagini, R. E., Smith, J. P., Sammons, D. L., MacKenzie, B. A., Striley, C. A. F., Robertson, S. K., & Snawder, J. E. (2004). Development of a sensitivity enhanced multiplexed fluorescence covalent microbead immunosorbent assay (FCMIA) for the measurement of glyphosate, atrazine and metolachlor mercapturate in water and urine. *Analytical and Bioanalytical Chemistry*, 379(3), 368-374.
- Borjesson, E., & Torstensson, L. (2000). New methods for determination of glyphosate and (aminomethyl)phosphonic acid in water and soil. *Journal of Chromatography A*, 886(1-2), 207-216.
- Bouvier, G., Blanchard, O., Momas, I., & Seta, N. (2006). Pesticide exposure of non-occupationally exposed subjects compared to some occupational exposure: A French pilot study. *Science of The Total Environment*, 366(1), 74-91.
- Bradberry, S. M., Proudfoot, A. T., & Vale, J. A. (2004). Glyphosate poisoning. *Toxicological Reviews*, 23(3), 159-167.

- Colborn, T., vom Saal, F. S., & Soto, A. M. (1993). Developmental effects of endocrine-disrupting chemicals in wildlife and humans. *Environmental Health Perspectives*, *101*(5), 378-384.
- Cooper, R. L., Stoker, T. E., Goldman, J. M., Parrish, M. B., & Tyrey, L. (1996). Effect of atrazine on ovarian function in the rat. *Reproductive Toxicology*, *10*(4), 257-264.
- Cooper, R. L., Stoker, T. E., Tyrey, L., Goldman, J. M., & McElroy, W. K. (2000). Atrazine Disrupts the Hypothalamic Control of Pituitary-Ovarian Function. *Toxicological Sciences*, *53*(2), 297-307.
- Courtney, K. D., & Moore, J. A. (1971). Teratology studies with 2,4,5-trichlorophenoxyacetic acid and 2,3,7,8-tetrachlorodibenzo-P-dioxin. *Toxicology and Applied Pharmacology*, *20*(3), 396-403.
- Croen, L. A., Todoroff, K., & Shaw, G. M. (2001). Maternal exposure to nitrate from drinking water and diet and risk for neural tube defects. *American Journal of Epidemiology*, *153*(4), 325-331.
- Curwin, B. D., Hein, M. J., Sanderson, W. T., Barr, D. B., Heederik, D., Reynolds, S. J., Alavanja, M. C. (2005a). Urinary and hand wipe pesticide levels among farmers and nonfarmers in Iowa. *Journal of Exposure Analysis and Environmental Epidemiology*, *15*(6), 500-508.
- Curwin, B. D., Hein, M. J., Sanderson, W. T., Nishioka, M. G., Reynolds, S. J., Ward, E. M., & Alavanja, M. C. (2005b). Pesticide contamination inside farm and nonfarm homes. *Journal of Occupational and Environmental Hygiene*, *2*(7), 357-367.
- Curwin, B. D., Hein, M. J., Sanderson, W. T., Striley, C., Heederik, D., Kromhout, H., Alavanja, M. C. (2007). Urinary pesticide concentrations among children, mothers and fathers living in farm and non-farm households in Iowa. *The Annals of Occupational Hygiene*, *51*(1), 53-65.
- Dallegrave, E., Mantese, F. D., Coelho, R. S., Pereira, J. D., Dalsenter, P. R., & Langeloh, A. (2003). The teratogenic potential of the herbicide glyphosate-Roundup in Wistar rats. *Toxicology Letters*, *142*(1-2), 45-52.
- Dill, G. M. (2005). Glyphosate-resistant crops: history, status and future. *Pest Management Science*, *61*(3), 219-224.
- Duke, S. O., & Powles, S. B. (2008). Glyphosate: a once-in-a-century herbicide. *Pest Management Science*, *64*(4), 319-325.

- Eskenazi, B., Bradman, A., & Castorina, R. (1999). Exposures of children to organophosphate pesticides and their potential adverse health effects. *Environmental Health Perspectives Supplements*, 107, 409.
- Frank, H. (2012). [Iowa Safe Drinking Water Information System].
- Franz, J., Mao, M. K., & Sikorski, J. A. (1997). Glyphosate: A unique global herbicide. (Monograph).
- Garry, V. F., Harkins, M. E., Erickson, L. L., Long-Simpson, L. K., Holland, S. E., & Burroughs, B. L. (2002). Birth defects, season of conception, and sex of children born to pesticide applicators living in the Red River Valley of Minnesota, USA. *Environmental Health Perspectives*, 110 Supplement 3, 441-449.
- Garry, V. F., Schreinemachers, D., Harkins, M. E., & Griffith, J. (1996). Pesticide applicators, biocides, and birth defects in rural Minnesota. *Environmental Health Perspectives*, 104(4), 394-399.
- Giesy, J. P., Dobson, S., & Solomon, K. R. (2000). Ecotoxicological risk assessment for Roundup herbicide. *Reviews of Environmental Contamination and Toxicology*, 167, 35-120.
- Golla, V. (2007). *Pesticide levels and absorbed doses inside Iowa homes over time: farm families' potential long-term exposures*. PhD, University of Iowa, College of Public Health, Department of Occupational and Environmental Health.
- Grube, A., Donaldson, D., Kiely, T., Wu, L. (2011). *Pesticides industry sales and usage: 2006 and 2007 market estimates*. United States Environmental Protection Agency Office of Chemical Safety and Pollution Prevention (7503P) EPA 733-R-11-001. Retrieved from www.epa.gov/pesticides.
- Hayes, T., Haston, K., Tsui, M., Anhthu, H., Haeffele, C., & Vonk, A. (2003). Atrazine-Induced Hermaphroditism at 0.1 ppb in American Leopard Frogs (*Rana pipiens*): Laboratory and Field Evidence. *Environmental Health Perspectives*, 111(4), 568.
- Hewitt, P., and Ganser, G.H. (2007). A Comparison of Several Methods for Analyzing Censored Data. *The Annals of Occupational Hygiene*, 51(7), 611-632.
- Hood, R. D., Patterson, B. L., Thacker, G. T., Sloan, G. L., & Szczech, G. M. (1979). Prenatal effects of 2,4,5-T, 2,4,5-trichlorophenol, and phenoxyacetic acid in mice. *Journal of Environmental Science and Health*, 13, 189-204.

- IDNR. (2010). Iowa Department of Natural Resources interactive mapping: pesticide sales. Retrieved from <http://programs.iowadnr.gov/ims/website/pesticide/Run.htm>.
- Kiely, T., Donaldson, D., & Grube, A. (2004). *Pesticide industry sales and usage: 2000 and 2001 market estimates*. United States Environmental Protection Agency Office of Prevention, Pesticides, and Toxic Substances (7503C) EPA-733-R-04-001. Retrieved from www.epa.gov/pesticides.
- Kniewald, J., Jakominić, M., Tomljenović, A., Šimić, B., Romac, P., Vranešić, Đ., & Kniewald, Z. (2000). Disorders of male rat reproductive tract under the influence of atrazine. *Journal of Applied Toxicology*, 20(1), 61-68.
- Kolpin, D., Furlong, E. T., Meyer, M. T., Thurman, E. M., Zaugg, S. D., Barber, L. B., & Buxton, H. T. (2002). Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in U.S. Streams, 1999–2000: A National Reconnaissance. *Environmental Science and Technology*, 36(6), 1202-1211.
- Kolpin, D., Thurman, E., Lee, E., Meyer, M., Furlong, E., & Glassmeyer, S. (2006). Urban contributions of glyphosate and its degradate AMPA to streams in the United States. *The Science of the Total Environment*, 354(2-3), 191-197.
- Kristensen, P., Irgens, L. M., Andersen, A., Bye, A. S., & Sundheim, L. (1997). Birth defects among offspring of Norwegian farmers, 1967-1991. *Epidemiology*, 8(5), 537-544.
- Kross, B. C., Hallberg, G. R., Bruner, D. R., Libra, R. D., Rex, K. D., Weih, L. M., & Hughes, J. P. (1990). The Iowa State-wide Rural Well-water Survey (SWRL): Water Quality Data: Initial Analysis (pp. 142): Iowa Department of Natural Resources, Geological Survey Bureau.
- Lin, N., & Garry, V. F. (2000). In vitro studies of cellular and molecular developmental toxicity of adjuvants, herbicides, and fungicides commonly used in Red River Valley, Minnesota. *Journal of Toxicology and Environmental Health. Part A*, 60(6), 423-439.
- Mendas, G. (2000). Determination of chloro- and methylthiothiazine compounds in human urine: extraction with diethyl ether and C18 solid-phase extraction for gas chromatographic analysis with nitrogen-selective and electron capture detection. *Analytica Chimica Acta*, 424(1), 7-18.
- Mesnage, R., Clair, E., Spiroux de Vendomois, J., & Seralini, G. E. (2009). Two cases of birth defects overlapping the Stratton-Parker syndrome after multiple pesticide exposure. *Occupational and Environmental Medicine*, 67(5), 359.

- Motojyuku, M., Saito, T., Akieda, K., Otsuka, H., Yamamoto, I., & Inokuchi, S. (2008). Determination of glyphosate, glyphosate metabolites, and glufosinate in human serum by gas chromatography-mass spectrometry. *Journal of Chromatography B, Analytical Technologies in the Biomedical and Life Sciences*, 875(2), 509-514.
- Munger, R., Isacson, P., Hu, S., Burns, T., Hanson, J., & Lynch, C. F. (1992). Birth defects and pesticide-contaminated water supplies in Iowa. *American Journal of Epidemiology*, 136, 959.
- Munger, R., Isacson, P., Hu, S., Burns, T., Hanson, J., Lynch, C. F., & Hausler, W. J., Jr. (1997). Intrauterine growth retardation in Iowa communities with herbicide-contaminated drinking water supplies. *Environmental Health Perspectives*, 105(3), 308-314.
- Murray, J. C. (2002). Gene/environment causes of cleft lip and/or palate. *Clinical Genetics*, 61(4), 248-256.
- NIDCR. (2010). *Prevalence of cleft lip and cleft palate*.
<http://www.nidcr.nih.gov/DataStatistics/FindDataByTopic/CraniofacialBirthDefects/PrevalenceCleftLip+LipCleftPalate.htm> (accessed November 24, 2012).
- NIOSH. (2002). Protecting Workers' Families - DHHS(NIOSH) Pub No. 2002-113 Retrieved Web Page, 2010, from <http://www.cdc.gov/niosh/docs/2002-113/2002-113.html>
- NRC. (1999). *Hormonally Active Agents in the Environment*: The National Academies Press.
- Olsson, A. O., Baker, S. E., Nguyen, J. V., Romanoff, L. C., Udunka, S. O., Walker, R. D., & Barr, D. B. (2004). A Liquid Chromatography–Tandem Mass Spectrometry Multiresidue Method for Quantification of Specific Metabolites of Organophosphorus Pesticides, Synthetic Pyrethroids, Selected Herbicides, and DEET in Human Urine. *Analytical Chemistry*, 76(9), 2453-2461.
- Paganelli, A., Gnazzo, V., Acosta, H., López, S. L., & Carrasco, A. s. E. (2010). Glyphosate-Based Herbicides Produce Teratogenic Effects on Vertebrates by Impairing Retinoic Acid Signaling. *Chemical Research in Toxicology*, 23(10), 1586-1595.
- Pellizzari, E. D., Smith, D. J., Andrew, C. C., & Quackenboss, J. J. (2003). Assessment of data quality for the NHEXAS Part II: Minnesota children's pesticide exposure study (MNCPEs). *Journal of Exposure Analysis and Environmental Epidemiology*, 13(6), 465-479.

- Picó, Y., Fernández, M., Ruiz, M. J., & Font, G. (2007). Current trends in solid-phase-based extraction techniques for the determination of pesticides in food and environment. *Sample Preparation*, 70(2), 117-131.
- Poole, C. F. (2007). Matrix-induced response enhancement in pesticide residue analysis by gas chromatography. *Data Analysis in Chromatography*, 1158(1-2), 241-250.
- Quackenboss, J. J., Pellizzari, E. D., Shubat, P., Whitmore, R. W., Adgate, J. L., Thomas, K. W., & Sexton, K. E. N. (2000). Design strategy for assessing multi-pathway exposure for children: the Minnesota Children's Pesticide Exposure Study (MNCPEs). *Journal of Exposure Analysis and Environmental Epidemiology*, 10(2), 145-158.
- Reddy, K. N., Rimando, A. M., Duke, S. O., & Nandula, V. K. (2008). Aminomethylphosphonic acid accumulation in plant species treated with glyphosate. *Journal of Agricultural and Food Chemistry*, 56(6), 2125-2130.
- Richard, S., Moslemi, S., Sipahutar, H., Benachour, N., & Seralini, G. E. (2005). Differential effects of glyphosate and roundup on human placental cells and aromatase. *Environmental Health Perspectives*, 113(6), 716-720.
- Ritchie, J. M., Vial, S. L., Fuortes, L. J., Guo, H., Reedy, V. E., & Smith, E. M. (2003). Organochlorines and risk of prostate cancer. *Journal of Occupational and Environmental Medicine*, 45(7), 692-702.
- Rodriguez, V. M., Thiruchelvam, M., & Cory-Slechta, D. A. (2005). Sustained exposure to the widely used herbicide atrazine: altered function and loss of neurons in brain monoamine systems. *Environmental Health Perspectives*, 113(6), 708-715.
- Romitti, P. A., Herring, A. M., Dennis, L. K., & Wong-Gibbons, D. L. (2007). Meta-Analysis: Pesticides and Orofacial Clefts. *The Cleft Palate-Craniofacial Journal*, 44(4), 358-365.
- Sagiv, S. K., Thurston, S. W., Bellinger, D. C., Tolbert, P. E., Altshul, L. M., & Korrick, S. A. (2010). Prenatal Organochlorine Exposure and Behaviors Associated With Attention Deficit Hyperactivity Disorder in School-Aged Children. *American Journal of Epidemiology*, 171(5), 593-601.
- Savitz, D. A., Arbuckle, T., Kaczor, D., & Curtis, K. M. (1997). Male pesticide exposure and pregnancy outcome. *American Journal of Epidemiology*, 146(12), 1025-1036.

- Schreinemachers, D. M. (2010). Perturbation of lipids and glucose metabolism associated with previous 2,4-D exposure: a cross-sectional study of NHANES III data, 1988-1994. *Environmental Health*, 26(9), 11-16.
- Simcox, N. J., Fenske, R. A., Wolz, S. A., Lee, I. C., & Kalman, D. A. (1995). Pesticides in household dust and soil: exposure pathways for children of agricultural families. *Environmental Health Perspectives*, 103(12), 1126-1134.
- Stillerman, K. P., Mattison, D. R., Giudice, L. C., & Woodruff, T. J. (2008). Environmental exposures and adverse pregnancy outcomes: a review of the science. *Reproductive Sciences*, 15(7), 631-650.
- Sulik, K. K., Cook, C. S., & Webster, W. S. (1988). Teratogens and craniofacial malformations: relationships to cell death. *Development*, 103(Supplement), 213-232.
- Ternes, T. A., Kreckel, P., & Mueller, J. (1999a). Behaviour and occurrence of estrogens in municipal sewage treatment plants — II. Aerobic batch experiments with activated sludge. *Science of The Total Environment*, 225(1-2), 91-99.
- Ternes, T. A., Stumpf, M., Mueller, J., Haberer, K., Wilken, R. D., & Servos, M. (1999b). Behavior and occurrence of estrogens in municipal sewage treatment plants — I. Investigations in Germany, Canada and Brazil. *Science of The Total Environment*, 225(1-2), 81-90.
- Theodoridis, G., Koster, E. H. M., & de Jong, G. J. (2000). Solid-phase microextraction for the analysis of biological samples. *Journal of Chromatography B: Biomedical Sciences and Applications*, 745(1), 49-82.
- Tian, Y., Ishikawa, H., Yamaguchi, T., Yamauchi, T., & Yokoyama, K. (2005). Teratogenicity and developmental toxicity of chlorpyrifos: Maternal exposure during organogenesis in mice. *Reproductive Toxicology*, 20(2), 267-270.
- Tomlin, C. D. (2006). *The Pesticide Manual: A World Compendium* (14th ed.). Hampshire, UK: British Crop Protection Council.
- USDA. (2007). *Agricultural chemical applications*. United States Department of Agriculture. Retrieved from <http://www.nass.usda.gov>.
- USDA. (2008). *National Agricultural Statistics Service*. United States Department of Agriculture. Retrieved from <http://www.nass.usda.gov>.

- USEPA. (2012a). *Safe Drinking Water Act, 40 CFR*. United States Environmental Protection Agency. Retrieved from <http://www.epa.gov/lawsregs/laws/sdwa.html>.
- USEPA. (2012b). *U.S. EPA Pesticides Program*. United States Environmental Protection Agency. Retrieved from <http://www.epa.gov/pesticides/>.
- Vencill, W. K. (2002). *Herbicide Handbook* (8th ed.). Lawrence, KS, USA: Weed Science Society of America.
- Weselak, M., Arbuckle, T. E., Wigle, D. T., Walker, M. C., & Krewski, D. (2008). Pre- and post-conception pesticide exposure and the risk of birth defects in an Ontario farm population. *Reproductive Toxicology*, 25(4), 472-480.
- Williams, G. M., Kroes, R., & Munro, I. C. (2000). Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. *Regulatory Toxicology and Pharmacology*, 31(2 Pt 1), 117-165.
- Winchester, P. D., Huskins, J., & Ying, J. (2009). Agrichemicals in surface water and birth defects in the United States. *Acta Pædiatrica*, 98(4), 664-669.