การประเมินความเสี่ยงต่อสุขภาพของประชาชนในอำเภอร่อนพิบูลย์ จังหวัดนครศรีธรรมราช จากการได้รับสารหนู

นายปิยวัฒน์ สายพันธุ์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต
สาขาวิชาสัตวแพทยสาธารณสุข ภาควิชาสัตวแพทยสาธารณสุข
คณะสัตวแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2551

HEALTH RISK ASSESSMENT FOR PEOPLE IN RONPHIBUN DISTRICT, NAKHON SI THAMMARAT PROVINCE FROM EXPOSURE TO ARSENIC

Mr. Piyawat Saipan

A Dissertation Submitted in Partial Fulfillment of the Requirements

for the Degree of Doctor of Philosophy Program in Veterinary Public Health

Department of Veterinary Public Health

Faculty of Veterinary Science

Chulalongkorn University

Academic year 2008

Thesis Title	HEALTH RISK ASSESSMENT FOR PEOPLE IN RONPHIBUN DISTRICT, NAKHON SI THAMMARAT PROVINCE FROM EXPOSURE TO ARSENIC
By	Mr. Piyawat Saipan
Field of Study	Veterinary Public Health
Advisor	Assistant Professor Suthep Ruangwises, Ph.D.

Accepted by the Faculty of Veterinary Science, Chulalongkorn University in Partial Fulfillment of the Requirements for the Doctoral Degree

Annop Kunavongkrit ..... Dean of the Faculty of Veterinary Science

(Professor Annop Kunavongkrit, Ph.D.)

THESIS COMMITTEE

..... Chairman

(Associate Professor Alongkorn Amonsin, Ph.D.)

Suthep Ruangwises ..... Advisor

(Assistant Professor Suthep Ruangwises, Ph.D.)

S. Nuanualsuwan ..... Member

(Assistant Professor Suphachai Nuanualsuwan, Ph.D.)

Komkrich P. ..... External Member

(Associate Professor Komkrich Pimpukdee, Ph.D.)

Nongluck R. ..... External Member

(Assistant Professor Nongluck Ruangwises, Ph.D.)

ปิยวัฒน์ สายพันธุ์ : การประเมินความเสี่ยงต่อสุขภาพของประชาชนในอำเภอร่อนพิบูลย์ จังหวัดนครศรีธรรมราช จากการได้รับสารหนู (HEALTH RISK ASSESSMENT FOR PEOPLE IN RONPHIBUN DISTRICT, NAKHON SI THAMMARAT PROVINCE FROM EXPOSURE TO ARSENIC) อ. ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ. ดร. สุเทพ เรืองวิเศษ, 200 หน้า.

การศึกษาครั้งนี้มีวัตถุประสงค์เพื่อประเมินปริมาณการบริโภคดินของคนไทยและประเมินความเสี่ยงจากการได้รับสารหนูจากการบริโภคดินและบริโภคอาหาร การประเมินการบริโภคดินศึกษาทั้งในเด็กและผู้ใหญ่ โดยวัดปริมาณ Aluminum (Al), Silicon (Si) และ Yttrium (Y) จากการเก็บตัวอย่างอาหารด้วยวิธี Duplicate meal sampling พร้อมทั้งสิ่งขับถ่ายจากอาสาสมัครเป็นเวลาติดต่อกัน 7 วัน วิเคราะห์ปริมาณสาร 3 ชนิดด้วย Inductively coupled plasma-atomic emission spectrometry (ICP-AES) และใช้วิธี Mass balance approach เพื่อประเมินการบริโภคดิน พบว่าค่าเฉลี่ยและเปอร์เซนต์ไทล์ที่ 95 การบริโภคดินในเด็กที่ได้จากการวิเคราะห์ Al มีค่า 29.88 และ 190.94 มิลลิกรัม/วัน ที่ได้จากการวิเคราะห์ Si มีค่า 36.33 และ 173.35 มิลลิกรัม/วัน และที่ได้จากการวิเคราะห์ Y มีค่า 30.05 และ 157.38 มิลลิกรัม/วัน (n = 70) ในผู้ใหญ่ค่าเฉลี่ยและเปอร์เซนต์ไทล์ที่ 95 การบริโภคดินที่ได้จากการวิเคราะห์ Al เท่ากับ 27.16 และ 106.7 มิลลิกรัม/วัน ที่ได้จากการวิเคราะห์ Si มีค่า 22.53 และ 127.39 มิลลิกรัม/วัน และที่ได้จากการวิเคราะห์ Y มีค่า 23.47 และ 114.77 มิลลิกรัม/วัน (n = 70) ผู้วิจัยแนะนำให้ใช้อัตราการบริโภคดินเฉลี่ย 50 มิลลิกรัม/วัน และค่า 95 เปอร์เซนต์ไทล์เท่ากับ 175 มิลลิกรัม/วัน สำหรับเด็ก และในผู้ใหญ่แนะนำให้ใช้ค่า 35 และ 120 มิลลิกรัม/วัน ตามลำดับ การประเมินความเสี่ยงจากการได้รับสารหนูโดยเก็บตัวอย่างดินในพื้นที่อำเภอร่อนพิบูลย์เพื่อวิเคราะห์ปริมาณสารหนูโดยวิธี Hydride generation-atomic absorption spectrometry (HG-AAS) (n = 59) ในการประเมินความเสี่ยงทั้งแบบเชิงกำหนดและเชิงความน่าจะเป็น พบว่า Hazard quotient ในเด็กมีค่าระหว่าง 0.32 - 5.46 และ 0.38 – 9.0 ในผู้ใหญ่ และ Cancer risk ในเด็กมีค่าระหว่าง 4.14×10^{-6} - 1.4×10^{-4} และในผู้ใหญ่คือ 1.25×10^{-5} - 3.7×10^{-4} การได้รับสารหนูจากการบริโภคอาหารโดยเก็บตัวอย่างด้วยวิธี Duplicate meal method จากอาสาสมัครเป็นเวลา 7 วันต่อเนื่องกัน (n = 112) วิเคราะห์ปริมาณสารหนูโดยวิธี HG-ASS พบว่า Hazard index มีค่าระหว่าง 3.16 – 13.24 และ Total cancer risk มีค่าระหว่าง 7.25×10^{-4} - 3.97×10^{-3} ค่าเฉลี่ยของความเสี่ยงที่ประเมินได้มาจากการบริโภคอาหาร 88% และทางการบริโภคดิน 12% จากการประเมิน sensitivity analysis พบว่า ระยะเวลาการได้รับสารและความเข้มข้นของสารหนูในอาหารเป็นปัจจัยสำคัญที่มีอิทธิพลต่อค่าความเสี่ยงที่ประเมิน โดยสรุปความเสี่ยงของประชาชนในอำเภอร่อนพิบูลย์จากการได้รับสารหนูมีค่าสูงเกินกว่าระดับที่ยอมรับได้

ภาควิชา.....สัตวแพทยสาธารณสุข..... ลายมือชื่อนิสิต.....

สาขาวิชา....สัตวแพทยสาธารณสุข.... ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์หลัก.....

ปีการศึกษา 2551

4775953231: MAJOR VETERINARY PUBLIC HEALTH

KEYWORDS: ARSENIC/ RONPHIBUN/ RISK ASSESSMENT

PIYAWAT SAIPAN: HEALTH RISK ASSESSMENT FOR PEOPLE IN RONPHIBUN DISTRICT, NAKHON SI THAMMARAT PROVINCE FROM EXPOSURE TO ARSENIC. ADVISOR: ASST. PROF. SUTHEP RAUNGWISES, Ph.D., 200 pp.

The purposes of the study were to determine the amount of soil ingested by Thai people and to conduct a risk assessment of people residing in Ronphibun district from consuming the arsenic contaminated food by duplicate meal method and soil ingestion pathway. Soil ingestions in Thai people were studied in both children and adults by using aluminum (Al), silicon (Si), and yttrium (Y) as trace elements. A mass balance approach was employed to assess daily soil ingestion. Duplicate samples of foods and beverages, feces, and urine were collected for 7 consecutive days. The amounts of tracer elements in samples were analyzed using inductively coupled plasma-atomic emission spectrometry (ICP-AES). In children, an average and the 95th percentile of soil ingestion based on Al were 29.88 and 190.94 mg/d, based on Si were 36.33 and 173.35 mg/d, and based on Y were 30.05 and 157.38 mg/d (n = 70). In adults, the average and the 95th percentile of soil ingestion based on Al were 27.16 and 106.7 mg/d, based on Si were 22.53 and 127.39 mg/d, and based on Y were 23.47 and 114.77 mg/d (n = 70). The recommended mean and the upper percentile of soil ingestion for Thai children were 50 and 175 mg/d and Thai adults were 35 and 120 mg/d, respectively. Both point and probabilistic risk assessment were used to estimate risk of ingested arsenic from soil in Ronphibun. Soil samples were taken from a land located in area and determined of arsenic concentration by hydride generation-atomic absorption spectrometry (HG-AAS) (n = 59). Hazard quotients were 0.32 - 5.46 in children and 0.38 – 9.0 in adults. The ranges of cancer risk from exposed to arsenic in soil were 4.14×10^{-6} - 1.4×10^{-4} in children and 1.25×10^{-5} - 3.7×10^{-4} in adults. Exposure to arsenic from food and water in adults was investigated by using 7 consecutive days duplicate meal samples collection from Ronphibun residents (n = 112). Inorganic arsenic concentrations are determined by HG-AAS. The ranges of total cancer risk were 7.25×10^{-4} - 3.97×10^{-3}. Hazard index ranged from 3.16 – 13.24. The averages of contributions to risk from and soil pathway were found to be 88% and 12%, respectively. Sensitivity analysis indicated that most influential of risk were exposure duration and arsenic concentration in meal. In conclusion, risk values for people in Ronphibun district from exposure to arsenic exceeded the risk level of concern.

Department :....Veterinary Public Health... Student's signature.....

Field of study :...Veterinary Public Health... Advisor's signature.....

Academic year :.....2008.....

ACKNOWLEDGEMENTS

I would like to express my highest gratitude to my major advisor, Asst. Prof. Dr. Suthep Ruangwises for his invaluable support and guidance throughout the course of this research. I am also grateful to my committee members; Assoc. Prof. Dr. Alongkorn Amonsin, Assoc. Prof. Dr. Komkrich Pimpukdee, Asst. Prof. Dr. Nongluck Ruangwises, and Asst. Prof. Dr. Suphachai Nuanualsuwan for improving this dissertation substantially.

Gratitude also goes to the following people: staffs of Ronphibun hospital, all the staff at ERTC, Mrs. Valasinee Rugkhaw for their cooperation and valuable assistance. I also wish to thank for Assoc. Prof. Dr. Monchai Duangjinda for help in explaining of the Monte Carlo statistics.

Great appreciation is extended to Ronphibun people for their time and willingness to participate in the study. They were a major source of data used in this study.

The financial support provided by the 90th Anniversary of Chulalongkorn University Fund (Ratchadaphiseksomphot Endowment Fund) during the course of my doctoral program is greatly appreciated.

Lastly, I am also greatly indebted to my parents, my special wife and my wonderful daughter for their continuous support and constant encouragement.

CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

>	Greater than
≥	Greater than or equal to
=	Equal to
<	Less than
≤	Less than or equal to
–	Negative
+	Positive
%	Percentage
µg	Microgram
MCA	Monte Carlo analysis
ADD	Average daily intake
AT	Averaging time
ATSDR	Agency for Toxic Substances and Disease Registry
BMD	Benchmark dose
BW	Body weight
C	Concentration
CDF	Cumulative distribution function
CI	Confidence interval
cm	Centimeter
CSF	Cancer Slope Factor
CTE	Central tendency estimate

d (s)	Day (s)
DRA	Deterministic risk assessment
ED	Exposure duration
EF	Exposure frequency
HI	Hazard Index
HQ	Hazard quotient
hr (s)	Hour (s)
IRIS	Integrated Risk Information System
kg	Kilogram
l	Liter
LADD	Lifetime average daily dose
LOAEL	Lowest-Observed-Adverse-Effect-Level
MF	Modifying factor
min(s)	Minute (s)
mg	Milligram
ml	Milliliter
NOAEL	No-Observed-Adverse-Effect-Level
P	Percentile
PDF	Probability density function
RRA	Probabilistic risk assessment
RfD	Reference Dose
RME	Reasonable maximum estimate
s	Second
TCR	Total cancer risk

UF	Uncertainty factor
U.S.EPA	U.S. Environmental Protection Agency
yr (s)	Year (s)

CHAPTER I

INTRODUCTION

1.1 Background

In 1987, human health problems in Ronphibun district were reported to the public when the first serious case of keratosis and hyperpigmentation was diagnosed on a resident who suffered from arsenical skin cancer. In the area, this sickness is called “Kai-Dam” because it has dermatological symptom of creating dark spots on the skin to a hardening of the skin into nodules, often on the palms and soles. The Ministry of Public Health investigated arsenic associated with keratosis and hyperpigmentation, during 1987 to 1988 were found that 1,150 cases identified as having arsenical skin lesions and 818 (85%) patients were recorded as residents in Ronphibun subdistrict. The reports in 1994 showed that 162 of 616 participants were identified as the patients with arsenical skin manifestations (prevalence rate of 26.3%). By the late 1990s, around 1,500 people have been diagnosed with arsenic related skin disorders (Choprapawon and Rodcline, 1997; DMS, 2003; Rakwong, 1999; Vitayavirasak, 1999; Williams et al., 1996, 1998).

In 2000, the epidemiological survey by Siripitayakunkit (2000) showed the prevalence rate of 24.7% by using the skin lesion for selection criteria. Similarity, the resulted from a health survey funded by SEARO (Regional Office for Southeast Asia, WHO) in August 2000 estimated that approximately 6,120 of potentially 24,665 exposed subjects showed symptoms of arsenicosis (SEARO, 2001). Many residents in the mining area suffered from the same dermatological signs that were related to the consumption of contaminated water. There have four highly arsenic contaminated villages in Ronphibun subdistrict that should be study in details (JICA, 2000; POD, 1998). Institutes of Thai Government and Foreign Governments studied the skin disease and concluded that arsenic contamination of the groundwater by the mining process that occurred in the area for a hundreds year, caused the disease. The people

in those villages used water which drains from the highly contaminated areas of Suan Jun and Ronna Mountains with arsenopyrite (DMS, 2003; DEP, 2005; JICA, 2000; Williams et al., 1996).

Arsenic binds with iron and sulfur to form arsenopyrite in natural rock and soil. In mining process, arsenopyrite was separated by using strong acid. This condition, inorganic acid compounds can easily be dissolved in the water and easily distributed into the environment. In oxygenated water, arsenic occurs as arsenate but under reducing conditions arsenite predominate. While in oxygenated soil, inorganic arsenic is present in the pentavalent forms. Therefore, airborne or soil ingested arsenic is mainly inorganic form (ATSDR, 2007; Cullen and Riemer, 1989; WHO, 2001; Williams et al., 1996).

At present, mining activities which related to arsenic contamination are banned by the Department of Mineral Resources. However, arsenic contamination caused by past mining activities remains in the area.

Available data showed that arsenic contamination in some food samples ranged from 0 to 76.94 mg/kg (Thailand standard, 2 mg/kg for total arsenic). The samples of water were range <0.002 to 5,100 µg/l (Thailand standard, 50 µg/L for drinking water) and the ranges of arsenic in soil were 0 to 5,300 mg/kg (Thailand standard, 3.9 mg/kg for agricultural and resident land) (ONEP, 2004; ThaiFDA, 2003). However, data on exposure to arsenic in drinking water, soil and food in available surveys were usually of total arsenic rather than of inorganic arsenic compounds and recently many people try to avoid drinking arsenic contaminated groundwater. Thus, the use of arsenic concentration in contaminated ground and well water to assess risk may lead to overestimation of the recent arsenic intake. Most data on concentrations of arsenic in food refer to total arsenic. Organic arsenic forms are generally much less toxic than the inorganic arsenic. Almost no information is available on the effects of organic arsenic compounds in human. Therefore, risk assessment was based on exposure to inorganic arsenic, only (ATSDR, 2007; IRIS, 1998; U.S.EPA, 1984; WHO, 2001).

Humans may be exposed to inorganic arsenic from four environmental matrices: air, water, food and soil. The average daily intake of arsenic per person in the affected area was estimated more than 90% coming from drinking water and food. Intake arsenic from air is usually much smaller than meals, while dermal absorption is a relatively minor route of exposure (Meacher et al., 2002). Evaluation of the risks involved has long been based on the arsenic contents in the raw products, but food is generally consumed after being subjected to processing, which could alter the chemical forms of arsenic. In arsenic endemic areas, most of the cooking processes used entail a significant increase in the inorganic arsenic concentration and consequently an increase in the toxicological risk for the exposed population. Thus, tests to risk assessment by food consumption should take account of ready to eat. The arsenic concentration may differ between uncooked and cooked food and according to the method of cooking. Other method sampling for estimated the daily arsenic intake can not take into account the effects of the cooking process or cooking water. To determine the actual intake, duplicate meal method is required (Bae et al., 2002; Dabeka et al., 1993; Mohri et al., 1990; Rahman et al., 2006; Tsuda et al., 1995).

Arsenic is consumed not only in water and food but also via soil. Soil ingestion is routinely estimated as part of a risk assessment of contaminated areas. Both children and adults exposed to arsenic through indirect pathway. In generally, children ingest more soil than adults because the behavior activity but adults are the largest proportion of a population potentially exposed to a contaminated site. Therefore, exposure from soil ingestion of adults and children may play a significant role in risk assessment. In children, we focused on children from 1 to 6 years of age for the risk assessment since this group is the most susceptible to hand to mouth behavior.

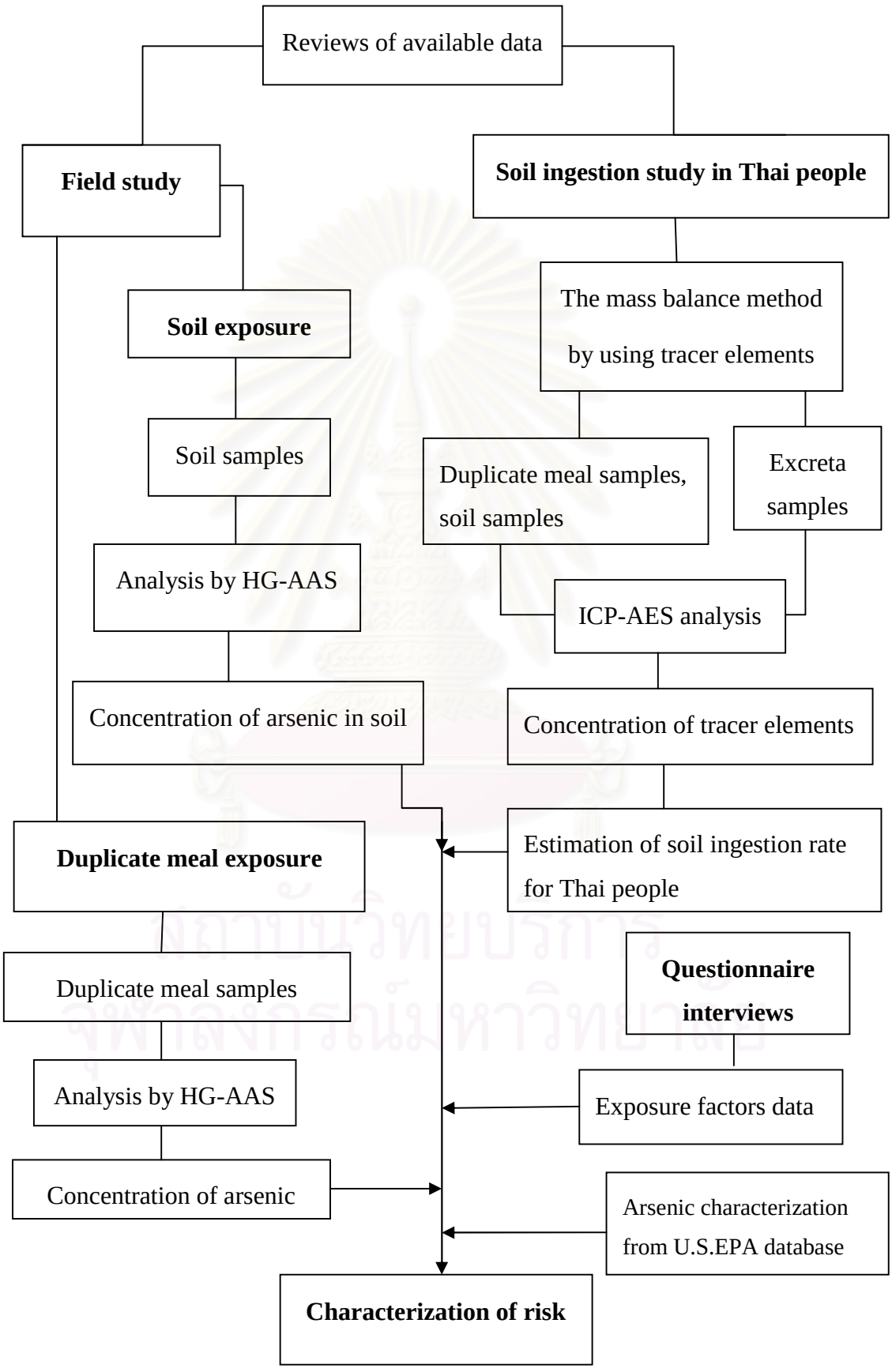
In Thailand, we have only one data of soil ingestion in Thai adults and two reported for children have published in 2003 (Khaokham, 2003; Pongkhamsing, 2003; Thermphonboon, 2003). All previous data to assess arsenic ingested soil in Ronphibun residents based on foreign studies. Exposed arsenic from soil ingestion within the population by using Thai data, should thus be viewed as a fundamental component of comprehensive risk assessment for this site. In addition, there are no

more studies on arsenic concentration in duplicate food in this region, so we can consider that the majority of arsenic in duplicate meal of this study may be present in the inorganic form. More data on ingested inorganic arsenic by duplicate meal and soil are needed to refine the human exposure assessment. May be, it is further recommended to propose a safety for arsenic exposure and risk manager to make better decisions for solving the problem in the future.

1.2 Framework of the study

This research was conducted in three major phases for approach arsenic risk assessment from consumption food and soil pathways (Figure 1.1). In soil ingestion phase, the studies were designed to estimate the amounts of soil ingested by Thai children and adults using the mass balance approach with aluminum, silicon and yttrium element. Field study phases, the studies were separated into two experiments. First, the investigation of arsenic concentration in soil was taken from Ronphibun district. Second, it was designed to estimate a consumption of arsenic from duplicate meal pathway. In part of interview application, an interview was conducted to analyze the exposure data which used to evaluate of risk from Ronphibun residents. Finally, all data were calculated for description of risk in terms of deterministic and probabilistic risk characterization from exposure to arsenic contaminated in soil (both children and adults) and duplicate meal (adults only) pathways.

Figure 1.1 Framework of the study



1.3 Purposes of the study

To assess the risks on human health associated with inorganic arsenic intake from food, water, and soil. Target cancer risk and hazard quotient values should be calculated based on the inorganic arsenic level in all media. It has become clear that dietary exposure can contribute significantly to the total daily intake of inorganic arsenic. More data on inorganic levels in food and soil consumption are needed to refine for human exposure assessment in Ronphibun area.

The present study has four main objectives: (1) to determine the amount of soil ingested by Thai adults; (2) to estimate of soil ingestion rate in children. The results of the first and second objectives are used to evaluate arsenic risk assessment from expose to soil in Ronphibun area; (3) to calculate a exposure assessment of inorganic arsenic via soil ingestion pathway and to characterize of risk in children from expose contaminated arsenic in soil; and (4) to estimate of inorganic arsenic intakes and to conduct a risk assessment from consuming the arsenic contaminated food by duplicate meal method and soil pathway in adults who living in an arsenic affected district of Ronphibun both deterministic risk assessment and probabilistic risk assessment approaches. Finally, it is to answer the key question “Does the probability of risk estimate exceed the risk level of concern?”

CHAPTER II

LITERATURE REVIEWS

2.1 Introduction

Ronphibun district is located approximately 840 km south of Bangkok in Nakhon Si Thammarat province, Southern Thailand and 32 kilometers south of Nakhon Si Thammarat city (Figure 2.1 and 2.2). It extends between longitudes 95º45' and 100º00' east and latitudes 8º00' and 8º15' north. The district has 6 subdistricts, which are further subdivided into 61 villages with population of 82,754 (Chantarawijit et al., 2000; DEP, 2005).

The town lies within the Southeast Asia Tin Belt running from Indonesia to Burma. Tin and associated minerals are found in the granitic rocks. Mining activities were century started in Ronphibun district. Tin was from two areas; the first was on the Ron Na Suang Chan mountain, the western side from town. The second area is located at the foothill of the mountain range. The ore minerals are composed of cassiterite (SnO_2) and wolframite $(FeMn)WO_4$ mineralisation, with abundant arsenopyrite (FeAsS) and pyrite (FeS_2) (Fordyce et al., 1994; JICA, 2000; Wattanasen, 2000; Williams et al., 1996). The main minerals of cassiterite and arsenopyrite were separated by roasting and using sulphuric acid and xyanthate. Enriched cassiterite was sent to a refining plant in Ronphibun subdistrict. There was a precipitation pond in the dressing plant that is suspected waste from dressing processes was sent to this pond to deposit large particle and then discharged to river. The minerals were separated by villagers who left the arsenopyrite widespread in the mountain range without any covering layer. The precipitation leached these waste into the environment and food crops may accumulated arsenic by root uptake from contaminated soil and water (Fordyce et al., 1994; JICA, 2000). Most of people in this site were agriculture. Agricultural productions were used consumed by themselves.

Figure 2.1 Regional location of Nakhon Si Thammarat Province

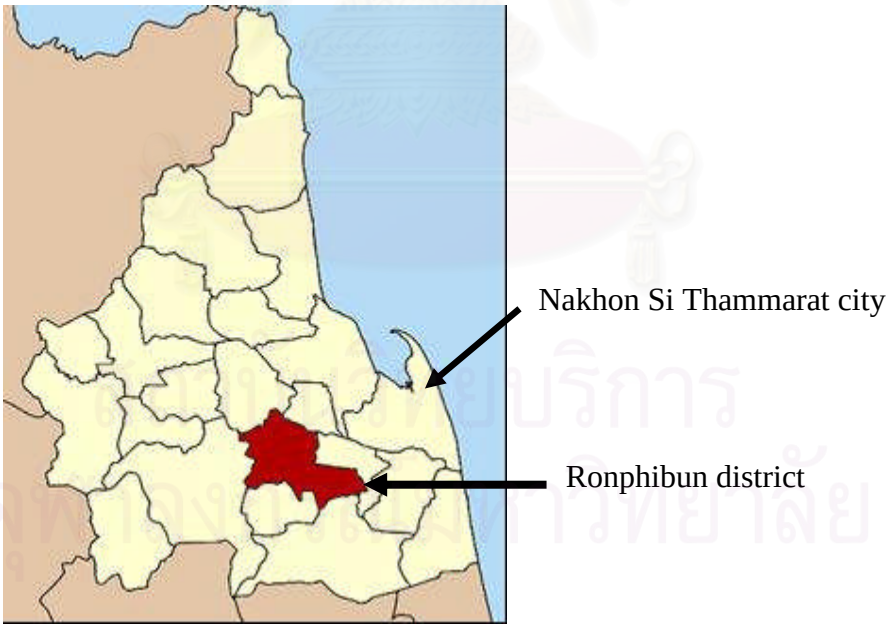


Figure 2.2 Regional location of Ronphibun district

Arsenic rich mining and processing waste piles reached into the river, coupled with the naturally high abundance (up to 0.5%) of disseminated arsenic in the alluvial deposits of the mid and lower catchment, has produced substantial contamination of shallow interstitial groundwater. Arsenic concentrations up to 5,000 µg/l have been found in groundwater (Williams et al., 1996). Groundwater has traditionally been used by residents in Ronphibun for all domestic purposes, and a statistical correlation has been demonstrated between the arsenic concentration of shallow well water at individual households and the body arsenic burdens of residents (Fordyce et al., 1994).

Four out of 16 villages of Ronphibun subdistrict with 30% of the population of the subdistrict account for 71% of the cases. Table 2.1 presents the number of arsenic patients in the subdistrict of Ronphibun. These villages used water which drained from the high contaminated area of Suan Jun and Ronna Mountains and wastes from dressing plants in town contaminant in the environment and food (JICA, 2000; Suwanmanee, 1990; Vitayavirasuk, 1999; Williams et al., 1996).

Table 2.1 Arsenicosis cases by village of residence

Village No.	No.of cases	Percentage	Village No.	No.of cases	Percentage
1	29	8.7	9	11	3.3
2	31	9.3	10	5	1.5
3	0	0	11	0	0
4	27	8.1	12	104	31.1
5	21	6.3	13	72	21.6
6	7	2.1	14	7	2.1
7	13	3.9	15	4	1.2
8	2	0.6	16	1	0.3

Source: (JICA, 2000)

The governmental agencies of Thailand have provided most of the population with safe drinking water by installing tube wells that exacted water from subsurface alluvial aquifers. However, some time it not enough for people demand. Arsenic contamination in food, water and soil samples from Ronphibun area are summarized in Section 2.3

Arsenic is a metalloid of the group VA elements in the periodic table, having both properties of a metal and a nonmetal with nitrogen, phosphorus, antimony and bismuth. However, it is frequently referred to as a metal. The atomic number and atomic weight of arsenic is 33 and 74.92, respectively. Chemically of arsenic closely resemble phosphorus. It is widely distributed in the Earth's crust, and has a steel grey metal-like color. Arsenics have no smell, and most have no special taste. Thus, people usually cannot tell if arsenic is present in food, water, or air. Arsenic is usually found in the environment combined with other elements such as oxygen, chlorine, and sulfur to form inorganic arsenic compounds, whereas in animals and plants arsenic combines with carbon and hydrogen to form organic arsenic compounds. Understanding the difference between inorganic and organic arsenic is important because some of the organic forms are less harmful than the inorganic forms. (ATSDR, 2007; U.S.EPA, 1984, 1988; WHO, 2001).

Depending on the geological environments arsenic can occur in four oxidation states as arsine (-3), arsenic metal (0), arsenites (+3) and arsenates (+5). The trivalent and pentavalent forms are the most common oxidation states. From the biological and the toxicological points of view can be classified arsenic compounds into three major groups; inorganic arsenic compounds, organic arsenic compounds and arsine gas. The most common trivalent inorganic compounds are arsenic trioxide, sodium arsenite and arsenic trichloride. Pentavalent inorganic compounds are arsenic pentoxide, arsenic acid and arsenates such as lead arsenate and calcium arsenate. Common organics arsenic compounds are arsinilic acid, methylarsonic acid, dimethylarsinic acid and arsenobetaine (HSDB, 2007). The chemical structure of some arsenic compounds are shown in Figure 2.3. In the case of risk assessment is concerned with the trivalent and pentavalent oxidation states because the common inorganic arsenic in water, food and

soil are probably arsenates and arsenites (Mandal and Suzuki, 2002; Mushak and Crocetti, 1995). Arsenic is a natural component of the Earth's crust. There are more than 245 species of arsenic bearing minerals. However, only three of them such as arsenic sulphide or realgar (As_2S_2), arsenic trisulphide or orpiment (As_2S_3) and arsenopyrite (FeAsS) are considered as arsenic ore because the amount of arsenic is higher in these three components (Pongratz, 1998; WHO, 2001). In Ronphibun, arsenopyrite has been identified as the major source of arsenic pollution.

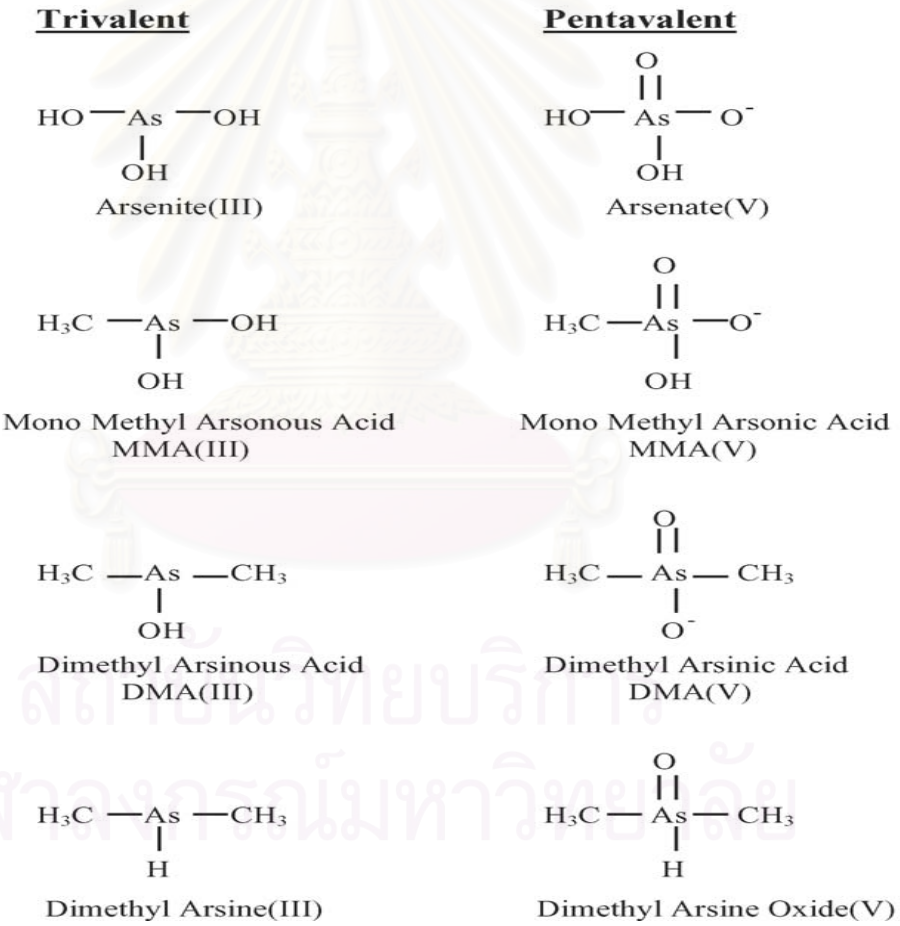


Figure 2.3 The most common arsenic compounds (Source: ATSDR, 2007)

Exposure to inorganic arsenic is a significant causal factor in human carcinogenesis and the development of a range of noncancer health effects in several countries with the most severe has been reported in worldwide. Exposure at contaminated sites may occur by a variety of pathways, including inhalation, ingestion of contaminated soil, water or through the food chain. The most common inorganic arsenic in water, food and soil are arsenite and arsenate. The magnitude of the exposures can only be evaluated on a site-by-site basis (U.S.EPA, 1989). Human may be exposed to arsenic organic by consumption of fish, shellfish or seafood in forms arsenobetaine and arsenocholine but there are insufficient human data to evaluate the toxicity. The organic forms of arsenic are not thought to be toxic and health effects data are not discussed in this thesis.

2.2 Sources and transformation of arsenic

Arsenics in the environment come from natural and anthropogenic sources. In natural sources arsenic is usually found at low concentration. They occur naturally in at least 245 mineral species; approximately 60% are arsenate, 20% are sulfides and sulfosalts and 20% includes arsenides, arsenites, oxides, silicates and elemental arsenic. Arsenic releases to water from weathering or leaching of arsenic rich rock and soil and accumulates in living organism (Garcia et al., 2002; Pongratz, 1998).

Anthropogenic sources, arsenic releases as a results of human activities such as the burning of coal, mining activities and the disposal of wastes from industrial activities. Large quantities of arsenic are also released from anthropogenic sources that play an important part in the contamination of the environment (IPCS, 2001; Nriagu, 1989). Arsenic problem in Ronphibun is classified that the contaminant from anthropogenic sources, being due to tin mining activities. There are three mineral dressing plants in Ronphibun district. The use of sulphuric acid and xyanthate in separated tin from other minerals, arsenic can broke from arsenopyrite and released into the environment. This has resulted in high concentrations of arsenic in surface water, groundwater, soil and vegetation (Smedley and Kinniburgh, 2002; Williams et

al., 1996). In strong acid conditions arsenate compound can easily be dissolved in water. An important reason for the arsenic to be easily distributed into the environment that is the use of sulphuric acid in the process ore dressing. The dry season is a preparatory stage in which arsenopyrites are exposed to air and oxidized. Dissemination of oxidized arsenic into river starts at the onset of the rainy season. The rainwater solubilize oxidized arsenic and disseminate them into the ecosystems through flood or storm water (Rodriguez et al., 2004). The flood in 1990s, it carried arsenic contaminant along Ronphibun area.

Arsenic cannot be destroyed in the environment, only its form can be changed. Arsenic in water and soil can undergo a series of transformations, including oxidation-reduction reactions, ligature exchange and biotransformation. Rate constants for these various reactions do not appear to be available (IPCS, 2001). In experimental data has been showed that a variety of vegetable crops accumulate arsenic by root uptake from soil or by absorption of airborne arsenic deposited on the leaves. Bioaccumulation of arsenic has been noted in some aquatic organisms such as algae and lower invertebrates that are consumed by predators. Some predators may accumulate inorganic arsenic and may thus represent a health risk (Helgesen and Larsen, 1998). Many incidents of contaminated arsenic in the environment have been reported in several counties. The situation can have significant adverse effects on health due to arsenic uptake in water and food especially in developing and rural population who depending on local sources of food and water (WHO, 2001).

2.3 Arsenic contamination in Ronphibun area

2.3.1 Water

In natural, arsenic primarily in its inorganic form is found in soil, air, and water. Water dissolves minerals that may release arsenic. Background levels of inorganic arsenic in seawater and fresh water ranged from 1 to 10 μg/l (WHO, 2001). However, many studies have been reported that the concentrations in several

groundwater samples ranged from 0.06 mg/l to 1.86 mg/l in affected arsenic area (Mandal and Suzuki, 2002; WHO, 2001).

The water samples from Ronphibun exceeded by 100 times of drinking water standard of Thailand, 0.05 mg/l. Table 2.2 summaries the amount of arsenic in water samples from this site. Concentrations of arsenic have been reported to range up to 5.5 mg/l in water. The governmental survey in 1987 found arsenic contents in the range from 0.05 to 4.45 mg/l. Village number 1, 2, 12 and 13 of Ronphibun subdistrict had water samples contaminated more than 0.2 mg/l and more than 25% of wells in these villages had arsenic levels exceeding 0.05 mg/l (Chongsuvivatwong et al., 2000; Choprapawon and Rodcline, 1997; Foy et al., 1992; PCD, 1998). The water monitoring survey in 1993 found that about 90% of shallow well samples had arsenic concentration more than 0.05 mg/l and there were hot spots in the soil with arsenic concentration exceeding 1,000 mg/kg. In 1986, eighty percent of cases used shallow well water for drinking. Approximately 9, 77, and 13% of drinking water were from shallow well, rainwater, and pipe water, respectively (Chongsuvivatwong et al., 2000; JICA, 2000; Oshikawa et al., 2007; Vitayavirasak, 1999; Vitayavirasak et al., 2005). Inorganic arsenic occurs in groundwater and most, > 80%, it is expected to be present as inorganic arsenic forms. Generally, it is assumed that nearly all arsenic in drinking water is inorganic (U.S.EPA, 1984).

Table 2.2 Summary results of total arsenic in water from Ronphibun samples

Year	Types of samples	Number of samples	Results, range(mean); mg/l	References*
1987	Pipe water	7	0.02-0.42 (0.1)	DMS (2002)
1987	Shallow water	1105	<0.05-3.66	DMS (2002)
1988	Shallow water	150	<0.05-4.45	DMS (2002)
1989	Shallow water	73	0 - 4	DMS (2002)
1990	Surface water	27	0.004-0.217	DMS (2002)
1991	Water	400	0.05-5.5 (1.3)	DMS (2002)
1992	Water	206	0.02-1.45 (0.24)	DMS (2002)
1992-1997	Surface water	560	0-1.6	DMS (2002)
1994	Drinking water	90	0-0.003	DMS (2002)
1995	Rain water	165	0-0.006	DMS (2002)
1997	Shallow water	72	<0.002-3.34	DMS (2002)
2000	Surface water	-	0.003-0.39	DMS (2002)

*DMS = Department of Medical Science, Thailand; reported until 2002 for submitted to WHO

Table 2.2 Summary results of arsenic in water from Ronphibun samples (continued)

Year	Types of samples	Number of samples	Results, range(mean); mg/L	References
1992	Shallow well	-	0.02-2.7 (0.82)	Foy et al. (1992)
1997	Water	-	0-0.246	Tongboriboon (1997)
2004	Water	72	< 0.002-0.66	Patarasiriwong and Wongpan (2004)

2.3.2 Soil

Arsenic is found primarily as arsenate in soil. Background arsenic in soil ranged from 0.2 to 40 mg/kg (WHO, 2001), although much higher levels may occur in mining areas, at waste sites, near high geological deposits of arsenic-rich minerals or from pesticide application. The natural level of arsenic in sediment is usually below 10 mg/kg of dry weight and varies considerably all over the world. The principal factors influencing the concentration of elements in soils are the parent rock and human activities (CCME, 1997; HSDB, 2007; Pongratz, 1998).

In Thailand, arsenic levels in soil have been provisionally established of 3.9 mg/kg for agricultural and residential lands and 27 mg/kg for other areas (ONEP, 2004) but arsenic content ranged from > 0 - 5,300 mg/kg in samples soil from Ronphibun (DMS, 2003; Visootiviseth et al., 2002; Williams et al., 1998).

Table 2.3 summarizes the concentration of arsenic in contaminated soils from various sites across Ronphibun. Analysis of soil indicated that most (>90%) of the arsenic in soil is inorganic (CCME, 1997; U.S.EPA, 1984). Concentrations of arsenic are highest in sediments near base metal mining and ore-processing operations. Average levels of 100 to 1,845 mg/kg (maximum 5,300 mg/kg) were reported near base metal mines in Ronphibun subdistrict (DMS, 2002). Analysis

of soil, water and plants from the Ronphibun district were collected in 1998-1999 showed that the area was widely contaminated with arsenic. Mine tailings contained up to 11,100 µg/g; soil samples ranged from 51 to 1,860 µg/g; and stream water ranged from 165 to 985 µg/ml (Visoottiviseth et al., 2002).

Table 2.3 Summary results of total arsenic in soil and sediment

Year	Types of samples	Number of samples	Results, range(mean); mg/kg	References*
1987	Soil	40	1.11-140.35 (28.34)	DMS (2002)
1992	Soil and sediment	205	50-5,300 (5,253)	DMS (2002)
1994	Soil	26	0-1,000 (168.1)	DMS (2002)
1995	Soil	25	0-1,770 (174.8)	DMS (2002)
1996	Soil	-	> 10 – 2,123	Williams et al. (1996)
2004	Surface soil	135	4.9-138.5	Patarasiriwong and Wongpan (2004)
2004	Ground soil	76	9.6-1,549	Patarasiriwong and Wongpan (2004)

*DMS = Data from Department of Medical Science, Thailand; reported until 2002 for submitted to WHO

2.3.3 Food

Food is generally the principal contributor to the daily intake of total arsenic. U.S.FDA (1997) estimated that at least 25% of the food consumption of arsenic from meats, poultry, dairy products, cereals, and tea were in the inorganic forms. Similarity the reports from WHO (2001) have found that the daily intake of total arsenic from food and beverages ranged from 20 to 300 µg/d. Limited data indicated that about 25% of the arsenic present in food was inorganic forms (WHO, 2001). The percentage of total arsenic that is inorganic in various foods has been determined to range 0% in saltwater fish to 75% in milk or dairy products, beef and pork. Available data indicated that about 90% of the arsenic in the edible parts of marine fish and shellfish is organic arsenic such as arsenobetaine, arsenochloline, dimethylarsinic acid, and that lower than 10% is inorganic arsenic (Benramdane et al., 1999; FSA, 2004; Li et al., 2003; Meacher et al., 2002; WHO, 2001).

The concentrations of arsenic in food from Ronphibun samples are summarized in Table 2.4. Some items found higher than 70 times with data in the previous sentence. Rakwong (1999) reported that freshwater snail from Ronphibun contain arsenic of 3.69 mg/kg while Thailand Food Standard Codes (ThaiFDA, 2003) has been established a maximum total arsenic limit of 2 mg/kg for all food except seafood. The determination of arsenic in 100 foods composites were collected from Ronphibun in 1999 to 2002. The highest mean concentrations of total arsenic were found in fish (1.89 µg/g), meat and poultry (1.2 µg/g) (DMS, 2002, 2003; Chantarawijit et al., 2000; PCD, 1998; Rakwong, 1999). Patarasiriwong and Wongpan (2004) found that turmeric, palm and coconut samples from Ronphibun area have inorganic form ranged from 24 to 66% of total arsenic.

Table 2.4 Summary concentration of total arsenic in foods

Year	Types of samples	Number of samples	Results, range(mean); mg/kg	References*
1987	Fruits, vegetables	13	0 - 1.62 (0.49)	DMS (2002)
1988	Plants and animals	65	0 - 1.3 (0.65)	DMS (2002)
1991	Fruits, vegetables	44	0 - 0.23	DMS (2002)
1993	Aquatic	136	0 - 76.94	DMS (2002)
1994	Duplicate meals	270	0.0002- 0.71	DMS (2002)
1996	Aquatic plants	32	0.86 - 2.97	DMS (2002)
1997	Aquatic animals	90	0.53 - 2.45	DMS (2002)
1998	Fish	-	0.02 - 4.15	DMS (2002)
1998	Fruits, vegetables	73	0 - 0.46	DMS (2002)
1997	Aquatic plants	-	0.23 - 2.97	Tongboriboon, 1997
2004	Fruits, vegetables	150	<0.005 - 0.87	Patarasiriwong and Wongpan (2004)

*DMS = Data from Department of Medical Science, Thailand; reported until 2002 for submitted to WHO

2.3.4 Arsenic accumulation in human

In human, it found that majority arsenic accumulates in the ectodermic tissue, primarily the hair and nail. The skin is known to localize and store arsenic because of its high keratin content which contains several sulfhydryl groups to which arsenite may bind and may be the reason for its sensitivity to arsenic toxic effect (Kitchin, 2001). The normal amount of arsenic in hair as about 0.08 - 0.25 µg/g with 1 µg/g being indication of the presence of excess arsenic and poisoning and normal arsenic concentration in nail is 0.34 ± 0.25 µg/g (Valentine et al., 1979). DMS (2002) have been reported that the ranges of arsenic in hair and nail were <0 to 45.5 mg/g and 1.32 to 100.2 mg/g, respectively. Because arsenic accumulated in keratin rich tissues such as skin, hair and nails, arsenic levels in hair and nails are used as indicators of part arsenic exposure (Hughes, 2006; OSHA, 2005).

2.4. Arsenic Biotransformation in Human

2.4.1 Absorption

Arsenic enters the body through ingestion, inhalation and skin absorption. The two major routes of absorption of arsenic are by ingestion and inhalation. Few investigations of dermal absorption rates for arsenic are undertaken and available data indicate that rates of absorption are lower than 10% (ATSDR, 2007; IRIS, 1998; OSHA, 2005). Wester et al. (1993) reported that human skin absorbed approximately 1 - 2% of the administered arsenical dose over 24 hrs period. Arsenic is well absorbed through the gastrointestinal tract into bloodstream. Several human studies indicated that arsenite and arsenate are well absorbed by oral route, the ranged from 40% to 100% (U.S.EPA, 1988; WHO, 2001; Zheng et al., 2002). The bioavailability of absorbed inorganic arsenic is dependent on the matrix media which it is exposed to.

The bioavailability of a chemical is the percentage of the ingested amount that is absorbed by the gastrointestinal tract. Arsenic in soluble form is generally assumed that its absorption from the gastrointestinal tract is nearly complete. However, arsenic in soil may be incompletely absorbed because they may be in insoluble forms or interact with other minerals (U.S.EPA, 1988, 1997b).

2.4.2. Distribution

After absorption, inorganic arsenic appears rapidly in the circulation, 90 to 95% of arsenic is located in erythrocytes. It bound to the globin in hemoglobin and is then transported to the other parts of the body. Many of the studies have used radiolabel arsenic, it showed that arsenic derived radioactivity is generally presented in all tissues examined. It is found mainly in the liver, kidney, lung, spleen and skin. Metallic elements may be stored in tissues both as inorganic species or salts and as species chelated to proteins and other organic compounds (ATSDR, 2007; IPCM, 1987; Roy and Saha, 2002; WHO, 2001).

Analysis of tissues taken at autopsy from people who were exposed of arsenic in food and water revealed that arsenic were presented in all tissues of the body. ATSDR (2007) reported that the high levels of arsenic were found in the liver, kidney, and brain during autopsy of an infant prematurely born to a young mother who had ingested inorganic arsenic at week 30 of gestation. Inorganic arsenic passes easily through the placenta. Similarity the reported by Concha et al. (1998) have been found arsenic concentration in cord blood and maternal blood (9 µg/l) of maternal exposed to high arsenic containing drinking water, 200 µg/l. Inorganic arsenic crosses the placental barrier and selectively accumulates in the neuroepithelium of the developing animal embryo. Following maternal exposure to arsenite or arsenate throughout gestation and lactation, inorganic arsenic and DMA were detected in the newborn mouse brains (ATSDR, 2007).

2.4.3 Metabolism

Inorganic arsenics are actively transported to the cell and the former by aquaglycoporins that normally transporting water and glycerol, the latter by the phosphate transporter. After entering the cell arsenate is rapidly reduced to arsenite (ATSDR, 2007; HSDB, 2007; IPCS, 2001).

In humans, metabolism of inorganic arsenic involves two basic processes. After entering the cell; the first process, inorganic arsenic is metabolized by reduction reactions that convert arsenate to arsenite. This reduction is a prerequisite for the methylation to occur. Arsenate is reduced to arsenite using glutathione to provide reducing equivalents or enzymatically by arsenate reductases. The relative contribution of each mechanism to arsenic reduction in mammalian species is not known with certainty (Concha et al., 2002; IPCS, 2001; Vahter, 2002).

The other process, methylation reactions which convert arsenite to mono-and dimethylated forms. Arsenite is methylated by enzymatic transfer of the methyl group from S-adenosylmethionine (SAM) to arsenite to form monomethylarsonic acid (MMA, V). MMA(V) can also be reduced by glutathione transferase to form monomethylarsenous acid (MMA, III). In a second methylation reaction MMA(III) forms dimethylarsinic acid (DMA,V). Subsequently, some DMA(V) is reduced to dimethylarsenous acid (DMA,III), followed by excretion in the urine of parent form, monomethylated and dimethylated compounds. The processes of inorganic arsenic metabolism are diagrammed in Figure 2.4. Reduction and oxidation between arsenates to arsenites forms takes place in the plasma, whereas methylation reactions occur primarily in the liver and to much lesser extent in the kidney and lung (IPCS, 2001; Mandal et al., 2004; Rossman, 2003; Roy and Saha, 2002; U.S.EPA, 1984, 1988; Vahter, 2002; WHO, 2001; Woffredo et al., 2003).

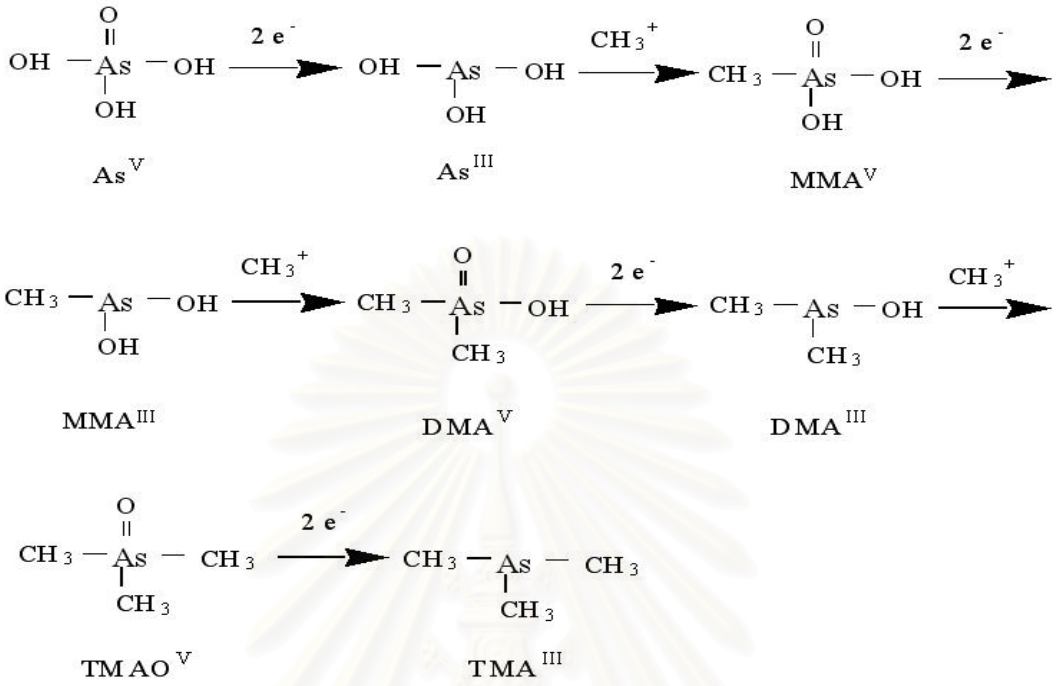


Figure 2.4 Inorganic arsenic metabolism (Source: ATSDR, 2007)

2.4.4 Excretion

The main route of excretion of arsenic after exposure to inorganic or organic arsenic species is urine, both in humans and in experimental animals. Smaller amounts are excreted in feces. Excretion is more rapid after exposure to arsenate than after exposure to arsenite, because the greater arsenite binding to protein thiol (-SH) groups (Calderon et al., 1999; Vahter, 2002; WHO, 2001).

There are two main processes for the elimination of ingested inorganic arsenic. The first is rapid excrete of non-methylated arsenic in both the trivalent and pentavalent forms. The second involves detoxification by sequential methylation of arsenite in the liver to dimethylarsinic acid (DMA) and monomethyarsonic acid (MMA). Excretion of the methylated compounds start approximately 5 hrs after ingestion but reaches its maximum level 2 to 3 days later. Studies with radioactively labeled arsenate in human shown about 38% of the dose was excreted in the urine

within 48 hrs and 58% of the total within 5 days (IPCS, 2001). In the subjects who ingested 500 µg of arsenite, 33% was excreted in the urine within 48 hrs and 45% within 4 days (Mandal and Suzuki, 2002). In women, who exposed to high concentration, 200 µg/l, of inorganic arsenic in drinking water. Arsenic has been excreted by breast milk with ranged from 0.08 to 8 µg/l (Concha et al., 1998; Sternowsky et al., 2002). The half-life of inorganic arsenic in human is estimated to be between 2 and 40 days. In humans, the relative proportions were usually about 40–75% of DMA, 20–25% of inorganic arsenic, and 15–25% of MMA (Concha et al., 2002; Hughes, 2006; IPCS, 2001; Uchino et al., 2006; U.S.EPA, 1988). Urinary arsenic concentrations in unexposed population are normally below of 50 µg/l. The urine samples were collected from residents in Ronphibun area found that 140 µg/l (DMS, 2003, PCD, 1998). Arsenic in urine can used to mark as short term exposure because after ingestion it has been excreted in a day.

2.4.5 Bioaccumulation

In general, concentrations of arsenic in organs tended to be higher after administration of arsenite than of because arsenate being a structural analogue of phosphate and substituting for it in the apatite crystal of bone. The greater retention of arsenite in tissues is a consequence of its reactivity and binding with tissue constituents, most notably sulfhydryl groups (IPCS, 2001). Farmer and Johnson (1990) reported that about 40 to 60% of arsenic may be retained in the body, mainly in the skin, hair, nails, muscle and small amounts in teeth and bones.

Nail, blood, urine, and hair have been considered for exposure monitoring. Nail and hair are the markers of longer exposure periods that have occurred over the past 6–12 months or more. They retain the highest concentration of arsenic due to the content of keratin, a group of proteins containing disulfide bonds. Urine and blood concentrations reflect recent intake, on the order of several days for urine and several weeks for blood based thus these markers are ideal for monitoring acute exposures (ATSDR, 2007).

2.5 Arsenic Toxicity in Human

2.5.1 Introduction of toxicity

The potency of arsenic toxicity is basically dependent on the form, inorganic or organic, and the oxidation state of the arsenic compounds. It is generally considered that inorganic arsenic are more toxic than organic arsenic. The toxicity of arsenic decrease in the order, arsines > arsenites > arsenoxides > arsenates > arsenic. Within these two classes, the trivalent oxidation state is more toxic than the pentavalent forms (ATSDR, 2007; Haupert et al., 1996; IPCS, 2001; NRC, 2001).

Many different possible modes of action of arsenate toxicity: to replace phosphate in glucose-6-phosphate and 6-phosphogluconate, to replace phosphate in the sodium pump and the anion exchange transport system of human red blood cells, to diminish the in vitro formation of adenosine-5-triphosphate (ATP) by replacing phosphate in enzymatic reactions, and to deplete ATP in some cellular systems, but not in human erythrocytes. The term of arsenolysis is arsenate disrupts the oxidative phophorylation process by arsenate replace phosphate in D-glyceraldehyde-3-phosphate to form 1-arsenato-3-phospho-D-glycerate which is unstable and it hydrolyzed to arsenate and 3-phosphoglycerate, thus the energy metabolism is inhibited and glucose-6-arsenate is producted rather than glucose-6-phosphate (ATSDR, 2007; Hughes, 2002; IPCS, 2001).

Trivalent inorganic arsenic is known to react with sulfhydryl groups, such as glutathione and cysteine. The complex between arsenic and sulfhydryl reagent is particularly strong. Arsenite replaces the two hydrogen atoms from thoil groups and attaches with a sulfur molecule and from dihydrolipoylarsenite chelate, which lead to the inhibition of essential biochemical reactions and alteration of cellular redox status. Arsenite inhibits pyruvate dehydrogenase, a complex that oxidizes pyruvate to acetyl coenzyme A, a precursor to intermediates of the citric acid cycle that provides reducing equivalents to the electron transport system for ATP production. As a result,

the amount of pyruvate in the blood increases, energy production is reduced and finally the cell damages. In the same way arsenic destroys workability of another enzyme and reduced production of succinyl coenzyme A and finally production of ATP is reduced. If arsenic is deposited for a long time, it breaks the ATP block for the energy supply to the cells (ATSDR, 2007).

Human are very sensitive to arsenic toxicity when compared with other experimental animals. For example, there is good evidence that arsenic is carcinogenic for humans but the evidence for animals is mostly negative (ATSDR, 2007; IPCS, 2001). Saha et al. (1999) reported that human oral exposure to inorganic arsenic of 0.05 – 0.1 mg/kg/d, causes neurological and hematological toxicity but not in monkeys, dogs and rats exposed to arsenite or arsenate at doses of 0.72 to 2.8 mg/kg/d. However, mechanisms of arsenic induced toxicity and carcinogenicity are not well understood. The mechanism of arsenic carcinogenicity is not known, the current view is functions as a promoter or cocarcinogen. (ATSDR, 2007; Chan and Huff, 1997; IARC, 1980; IRIS, 1998; U.S.EPA, 1988).

2.5.2 Non-carcinogenic toxicity

Arsenic can be toxic by interact with sulfhydryl groups of proteins and enzymes, to denature the proteins and enzymes within the cells and through an increase of reactive oxygen species in the cells consequently causing cell damage. Dose and exposure duration have an effect on the potential of arsenic toxicity. The lethal oral dose for human has been estimated from poisoning incidents to ranges from 70 to 300 mg arsenic (ATSDR, 2007). Dose of 0.05 mg/kg/d over weeks to months have caused gastrointestinal, hematological, hepatic, dermal, and neurological effects etc. Long terms exposure to drinking water at levels of 0.002 to 0.02 mg/kg/d have been associated with skin lesions and skin, bladder, kidney, and liver cancer (Ahmad et al., 1997; Ahsan et al., 2006; IRIS, 1998; Shannon and Strayer, 1989).

The short exposure results in acute effects characterized by vomiting, abdominal colic and diarrhea. Other effects can include muscular cramps and cardiac abnormalities, in rare cases these symptoms may be lead to vascular shock and death (OSHA, 2005; WHO, 2001). Chronic exposure may give rise to several health effects including effects on the gastrointestinal tract, circulatory system, respiratory tract, liver, kidney, skin, cardiovascular system, nervous system, hematopoietic system etc. One of the hallmarks of ingested inorganic arsenic toxicity is skin lesions such as hyperpigmentation and hyperkeratosis. The available data from humans identify the skin as the most sensitive biomarker of noncancinogenic effects relating from chronic oral arsenic exposure. The tolerable intake recommended by ATSDR, U.S.EPA, and WHO are based on drinking water studies in which the incidence of skin effects was observed to be related to arsenic intake. U.S.EPA selected the skin lesion for the endpoint of inorganic arsenic toxicity in human and it is used to evaluate the hazard characterization of inorganic arsenic (U.S.EPA, 1988).

2.5.3 Carcinogenic toxicity

Only inorganic arsenic is clear evidence of carcinogenic potential. No studies have been found concerning cancer in humans after ingestion of organic arsenic. Inorganic arsenics clearly have not mutagenic potential and there is some evidence for clastogenic effects in human. It was considered to be a promoter and cocarcinogen but not an initiator of carcinogenesis. In multistage carcinogenesis, mutations are important in initiation and progression during which malignancy and metastatic potential develops in a cell. While, cellular proliferation is an important driving force in promotion of carcinogenesis. The mode of action of arsenic is unclear, current understanding suggests that all proposed mechanisms occur via indirect mechanism. Arsenic induced carcinogenesis may involve several biological mechanisms including induced chromosomal abnormalities, oxidative stress, altered DNA repair, altered DNA methylation patterns, altered growth factors, enhanced cell proliferation,

promotion or progression, gene amplification and suppression of p53 (ATSDR, 2007; IPCS, 2001; Kitchin, 2001; Slayton et al., 1996; Smith et al., 1992).

Currently, three modes of action for arsenic carcinogenesis have a degree of positive evidence, both in experimental systems and in human tissues that induced chromosomal abnormalities, oxidative stress, and the combined of altered growth factors-cell proliferation-promotion.

Chromosomal abnormalities can be easily caused because of the tendency for trivalent arsenic forms to interact and disrupt the normal functioning of tubulin and spindles. It is the second, third and fourth steps of cancer causality that are weakest in the chromosomal abnormalities theory of arsenic carcinogenesis (ATSDR, 2007; IPCS, 2001). The oxidative stress theory partially depends on the ability of DMA or MMA metabolites to form free radicals. Recent mouse experiments showed rapid formation of free radicals after administration of arsenate or arsenite. Arsenic itself does not appear to induce point mutations but it induced genotoxicity may involve oxidants or free radical species. Alternatively, the inorganic forms of arsenic could directly generate free radicals. This can occur because arsenic changes oxidation states from trivalent to pentavalent depending on the exterior chemical environment (ATSDR, 2007; IPCS, 2001; Kitchin, 2001; Slayton et al., 1996). The combined theory of altered growth factors-cell proliferation-promotion of carcinogenesis is an excellent choice for a carcinogenic mode of action for arsenic. Increased concentration of growth factors can lead to cell proliferation and eventual promotion of carcinogenesis. Arsenic induced cell death can lead to compensatory cell regeneration and carcinogenesis. Altered growth factors, cell proliferation, and promotion of carcinogenesis have all been demonstrated in one or more systems exposed to arsenics. Altered growth factors and mitogenesis were found in human keratinocytes. Cell death was observed in human hepatocytes and rat bladder epithelium. Proliferation of cell was demonstrated in human keratinocytes and intact human skin and rodent bladder cells. Promotion of carcinogenesis was noted in rat bladder, kidney, liver, and thyroid, and mouse skin and lung (IPCS, 2001; Kitchin, 2001; Slayton et al., 1996; Smith et al., 1992).

2.6 Chemical Risk Assessment

2.6.1 Introduction

In 1983, the National Research Council (NRC) published risk assessment which outline the four basic steps of hazard identification, dose-response assessment, exposure assessment, and risk characterization. This outline is used until today. After the publication of NRC outline, U.S.EPA began issuing a series of guidelines for conducting risk assessments. In 1986, U.S.EPA issued final guidelines relating to risk assessment for cancer, mutagenic effects, developmental effects, exposure assessment, and chemical mixtures. Since 1986, U.S.EPA has updated or issued revised final guidelines for developmental toxicity, exposure assessment, reproductive toxicity, neurotoxicity, and ecological risk assessment. Today, in general guidance documents and policies used in other countries, the first three steps: hazard identification, dose-response assessment and exposure assessment are methodologically very similar to those practiced in U.S.EPA. However, the risk characterization step can vary across countries. In this study, risk assessment approach was carried out follow the U.S.EPA guidelines. Each of four steps of chemical risk assessment will be explained details in next Sections (NRC, 1983; U.S.EPA, 1989).

The basic definition of risk assessment is a process in which information is analyzed to determine if a hazard might cause adverse effects to human following exposure under defined conditions to a risk source. The term of hazard describes the potential of a risk source to cause an adverse effect and risk describes the probability and severity of an adverse effect occurring to human following exposure to a risk source. U.S.EPA uses it as a tool to integrate exposure and health effects information into a characterization of the potential for health hazards in humans and uses risk assessment as a source of scientific information for making decisions about managing risks to human health and the environment (U.S.EPA, 1989).

Briefly, all available evidence data in humans, experimental animals and in vitro possible adverse effects of the chemical are evaluated in hazard identification

step and weigh of evidence is considered whether adverse effect can be cause under exposure conditions existing for humans. Dose-response assessment, it performed based on data concerning relationship between exposure and adverse health effects. The exposure assessment seeks to determine the extent to which a population is exposed to the hazard. A description of exposure to the agents being considered is a very important component of risk assessment. Risk characterization is the combination of exposure assessment and dose-response assessment generates quantitative estimates of how many people exceed safety levels and describes the uncertainty and variability in these characterizations. As a result of risk assessment, further steps are often required in terms of risk control and risk management (U.S.EPA, 1989, 2000b).

2.6.2 Hazard identification

Hazard identification is determined whether exposure to chemical can cause an adverse effect and whether it effect is likely to occur in human. The hazardous properties of a chemical are assessed by a review of the human epidemiological and toxicological data derived from scientific or toxicity studies. Then, weight of evidence is considered whether specific adverse effects can be caused under exposure conditions existing for human. A weight of evidence approach uses all available toxicological, metabolic and physiochemical information about a compound for judging the likely potency of the compound in human. The utility of any overall risk assessment is critically dependent on the quality of this step.

Criteria that are generally applicable for judging the adequacy of mechanistically based data include: mechanistic relevance of the data to adverse effects, number of studies of each endpoint, consistency of results in different test systems and different species, similar dose-response relationships and mode of action-related effects, conduct of the tests in accordance with generally accepted protocols, and degree of consensus and general acceptance among scientists regarding interpretation of the significance and specificity of the tests. The weight of evidence

generally includes; conclusions about human adverse potentials, a summary of the key evidence supporting these conclusions, including information on the type of data used to support the conclusions, available information on the epidemiologic or experimental conditions that characterize expression of carcinogenicity, a summary of potential modes of action and how they reinforce the conclusions, indications of any susceptible populations or life stages (Smith, 2002).

The outcomes of hazard identification are systematically presented in many organizations such as NTP, IARC, IRIS, and ATSDR. U.S.EPA addresses the first two components, hazard identification and dose-response assessment, through its Integrated Risk Information System (IRIS). IRIS is now a publicly available repository of health effects information on 545 chemicals found in the environment. In case of inorganic arsenic, sufficient information showed that it is producing widely adverse effect both noncarcinogenic and carcinogenic effects to human and animals (IRIS, 1998).

2.6.3 Dose-response assessment

The objective of dose-response assessment or hazard characterization is to quantify the relationship between the exposure to the chemical and the extent of adverse effects, following the process of hazard identification. Data for dose response evaluations can be derived from epidemiological studies or from experimental animal studies. Risk assessment can not be done without good dose-response information. In general, adverse effect endpoint selection for using calculated dose-response value should be match the temporal and spatial characteristics of the exposure scenarios selected for use in the risk assessment. Toxicology endpoints for inorganic arsenic are skin disorder for noncarcinogenic effects and skin cancer for carcinogenic effects (OSHA, 2005; IRIS, 1998; U.S.EPA, 1988, 1989, 2000b).

The results of dose-response assessment for ingested toxicants are expressed in terms of reference dose (RfD) for non-carcinogenic effects and cancer slope factor (CSF) for carcinogenic effects. The RfD is defined as an estimate of a daily oral

exposure to the human population that likely to be without an risk of adverse effect. The CSF is expressed term of cancer potency. It is defined a slope factor as the upper bound, the 95th percentile, on the increased cancer risk from a lifetime exposure to toxicants. The details of dose response assessment are described below.

Dose-response assessment for noncarcinogenic effets: The concept of threshold level is used for noncancer characteristic. Scientists assumes that the protective mechanisms are believed to exist that must be overcome before the adverse effect is manifested. U.S.EPA has derived a chronic oral reference dose and reference concentration of 0.0003 mg/kg/d for inorganic arsenic based on a NOAEL of 0.0008 mg/kg/d for hyperpigmentation and keratosis in a Taiwanese exposed to arsenic in drinking water (Tseng 1977; Tseng et al. 1968). Their drinking water contained arsenic concentration of 0.001 - 0.127 mg/l. The concentration of 0.009 mg/l was taken as the NOAEL which was then adjusted to include an estimation of arsenic consumed in food (0.002 mg/d). Assuming a water intake of 4.5 l/d and average body weight of 55 kg produced a NOAEL of 0.0008 mg/kg/d. Then, the uncertainty factor of 3 was applied to account for both the lack of reproductive toxicity data and to all sensitivity population. Modifying factor was used default value of 1 for scientific judgment. Finally, the RfD of inorganic arsenic was 0.0003 mg/kg/d. Currently, the oral RfD derived in U.S.EPA is applicable to inorganic arsenic only (IRIS, 1998; NRC, 2001).

Dose response assessment for carcinogenic effects: The hypothesized mechanism is believed to be essentially no level of exposure to such a chemical that does not pose a finite probability of generating a carcinogenic response. This is referred to non threshold concept. U.S.EPA assumes that a small number of molecular events can evoke changes in a single cell that can lead to uncontrolled cellular proliferation and eventually to a clinical state of disease (U.S.EPA, 1984, 1988). Cancer slope factor (CSF) is the toxicity data most commonly used to evaluate potential human carcinogenic risks. CSF is expressed as the upper bound probability of developing cancer assuming continuous lifetime exposure to a substance at a dose of one milligram per kilogram of body weight, and is expressed in units of inverse dose as a potency slope (mg/kg/d). In case of arsenic, CSF is estimated form human

data. The current CSF for ingested inorganic is based on Taiwan epidemiological studies. (IARC, 1980; IPCS, 2001; U.S.EPA, 1984, 1988).

Taiwan studies (Tseng et al., 1968; Tseng, 1977) have several strengths for quantitative dose-response assessment including the number of the exposed population is large (40,412 people), the number of skin cancer cases is relatively large (428 cases) and the skin cancer prevalence rates are reported by twelve different age and dose groups. Skin cancer in Taiwan cases included squamous cell carcinoma and basal cell carcinoma. Based on these studies, U.S.EPA has estimated lifetime skin cancer risk associated with the ingestion of arsenic by using a multistage model modified and assumed no threshold to generate the estimated lifetime cancer risk as a maximum likelihood estimate. A generalized multistage model is employed to predict the prevalence of skin cancer as a function of arsenic concentration in drinking water (d) and age (t) assuming exposure to a constant dose rate. Let $F(t,d)$ represent the probability of developing skin cancer by age t after lifetime exposure to arsenic concentration d. The equation has forms following:

$$F(t,d) = 1 - \exp[-g(d)\,H(t)] \qquad \text{(Eq 2.1)}$$

where:

$g(d)$ = a polynomial in dose with non-negative coefficients

$H(t) = (t-w)^k$ where k is any positive real number, and t > w for induction time w.

The model $F(t,d)$ is a generalization of the multistage in which k can only assume the value of positive integers. The number of people at risk and the number with skin cancer at different values of t and d must be known in order to employ maximum likelihood estimation. Finally, the quantitative estimates of carcinogenic risk from inorganic arsenic oral exposures include a cancer slope factor of 1.5 per mg/kg/d (IRIS, 1998; U.S.EPA, 1988).

In conclusion, dose-response assessments of ingested inorganic arsenic are 0.0003 mg/kg/d for non-carcinogenic effects and 1.5 per mg/kg/d for carcinogenic effects. These values are used in risk characterization with combine to exposure assessment information in this study.

2.6.4 Exposure assessment

A description of exposure to the chemical is a very important component of risk assessment. The validity and reliability of any conclusion and advice to risk managers depends on the quality, reliability and relevance of the available exposure data. In contrast, estimation of intake can be a major source of uncertainty in the studies. The objective of the exposure assessment is to estimate the type and magnitude of exposures to the chemical of potentials concern that are present at a site. The results of the exposure assessment are combined with results of dose-response assessment, information to characterize potential risks (Graham et al., 1992; Licier and Schecter, 1998; Paustenbach, 2000).

Many sources of information for describe exposure assessment and risk characterization. In this present study is referenced throughout of U.S.EPA guidelines. The exposure assessment proceeds in three steps following setting of exposure characterized, identification of exposure pathways, and quantification of exposure. Characterize the exposure setting with respect to the general characteristics of the site and populations, activity patterns and the presence of sensitive subgroups. Next, exposure pathway identified the chemical agent takes from the source to the exposed individual. An exposure pathway analysis links the sources, locations, and types of environmental releases with population locations and activity patterns to determine the significant pathways of human exposure. Finally, the exposure assessment process is to quantify the magnitude, frequency and duration of exposure for the populations and exposure pathways selected for quantitative evaluation (U.S.EPA, 1997a, 2000c).

The estimation of chemical intakes used to three categories variable are exposure concentration variables (variables that describe the exposed population namely; contact rate, exposure frequency and duration) body weight, and assessment determined variable (averaging time). Briefly, exposure is dependent upon the concentration of contaminant, frequency and duration of contact. They are typically expressed in terms of concentration per unit or dose in the media to which humans are exposed. The most common measures are average daily dose (ADD) which is used to assess the noncancer effects of a chemical (Equation 2.2) and LADD for carcinogen effects (Equation 2.3).

$$\mathrm{ADD} = \frac{\mathrm{C\ x\ IR\ x\ AF\ x\ ED\ x\ EF}}{\mathrm{BW\ x\ ATnc}} \qquad (\mathrm{Eq.\ 2.2})$$

$$\mathrm{LADD} = \frac{\mathrm{C\ x\ IR\ x\ AF\ x\ ED\ x\ EF}}{\mathrm{BW\ x\ ATc}} \qquad (\mathrm{Eq.\ 2.3})$$

where:

ADD = average daily dose (mg/kg/d)

LADD = lifetime average daily dose (mg/kg/d)

C = exposure concentration (mg/g)

IR = ingestion rate (mg/d)

ED = duration of exposure (years)

EF = exposure frequency (days/year)

BW = body weight (kg)

AF = absorption factor (unitless)

ATnc = averaging time (days) for noncancer effects.

ATc = averaging time (days) for cancer effects.

All variables needed for model estimations are represented by the exposure parameters representing the so called exposure factors. Below, these are general variable that used to estimate oral intake based on U.S.EPA determination and used in this study.

Exposure concentration: It is the concentration of the contaminant in the medium such as food water or soil, contacting the body.

Intake rate: It refers to the rates of inhalation, ingestion, and dermal contact depending on the route of exposure. For ingestion, the intake rate is simply the amount of food containing the contaminant of interest that an individual ingests during some specific time period.

Exposure frequency and duration: They are used to estimate the total time of exposure. They are the length of time of contaminant contact.

Body weight: A constant body weight over the period of exposure is used primarily by convention but also because body weight is not always independent of the other variables in the exposure equation (most notably, intake). U.S.EPA (1997a) recommended that keeping body weight constant, error from this dependence is minimized. The average body weight is used because when combined with the other variable values in the intake equation, it is believed to result in the best estimate of the reasonable maximum estimate.

Averaging time: The time period over which the dose is averaged (days). The approach for carcinogens is based on the assumption that a high dose received over a short period of time is equivalent to a corresponding low dose spread over a lifetime.

Absorption factor: It describes the ratio of the absorbed fraction of a substance from a particular exposure medium relative to the fraction absorbed from the dosing vehicle used in the toxicity study for that substance.

The data required for assessing dietary exposure are determined by the objective of the assessment. Several methods can be used to estimate the intake of a contaminated food. U.S.EPA (1992) have been suggested that three different approaches in quantitative exposure estimation of chemicals namely; point of contact

measurement (the exposure can be measured concentration and time of point contact and integrating them), scenario evaluation (the exposure can be estimated by separately evaluating the concentration and the time of contact then combing this information), and biomarkers evaluation (the exposure can be estimated from dose which in turn can be reconstructed through internal indicators after the exposure has taken place). For examples, duplicate diet method is the point of contact measurements while food supply, acquisition and consumption are scenario evaluation.

Typically, U.S.EPA uses deterministic risk assessment (DRA) or point estimation approaches to characterize risk and applies probabilistic techniques for characterization of risk, usually within exposure assessment. Point estimate risk assessment uses single value to represent variables in a risk equation. A point estimate of risk can be a central tendency exposure (CTE) or reasonable maximum exposure (RME). CTE represents the average or typical individual in a population usually considered to be the mean or median. RME is defined as the highest exposure that is reasonably expected to occur at a site. The high end of exposure occurs between the 90^{th} - 99^{th} percentiles. The output of deterministic estimation is a point of risk. Probabilistic risk assessment (PRA) is a general term for risk assessment that use probability models to represent the likelihood of different risk levels in population and to characterize uncertainty in risk estimates. Probabilistic analysis uses probability distribution for variables in a risk equation in order to quantitatively characterize variability and uncertainty. The output of probabilistic risk assessment is a probability distribution of risk. Since the results of point estimation generally do not lend more characterize of variability and uncertainty to assessors. Probabilistic approach of risk assessment is receiving increasing attention both regarding exposure assessment and risk characterization (U.S.EPA, 2000b, 2001a).

Probabilistic analyses have been recognized in regulatory guidance and U.S.EPA has published a document of principles for conducting Monte Carlo analyses. Monte Carlo analysis (MCA) refers to a technique for characterizing the uncertainty and/or variability in risk estimates by repeatedly sampling the probability

distributions of the risk equation inputs and using these inputs to calculate a range of risk values. Monte Carlo model accounts for the uncertainty in select parameters evaluating the range and probability of plausible exposure levels. Instead of specifying input parameters as single values this model allows for consideration of the probability distribution (U.S.EPA, 1995, 2001a). The process of setting up and running the models of Monte Carlo simulation requires appropriate modeling software and a high level of computer processing power. There are a variety of risk analysis software products on the market. Examples of software products are @RISK (Palisade, USA) and Crystal ball (Decisioneering, USA). In the process, the variables of a model can be defined in terms of a probability density function (PDF). A PDF is a mathematical formula that describes how frequently a variable will have any specific value or range of values. There are various types of PDF such as normal, lognormal, uniform, and triangular distributions. Each PDF is completely specified by one or more parameters. For example, normal and lognormal PDFs are specified by the mean (μ) and standard deviation (σ) of a sample drawn from the population. Monte Carlo method incorporates the ranges or distributions of data associated with the risk model. Because a computer can evaluate thousands of combinations of exposure variables, the probability of occurrence of any of these combinations can be easily ranked and the resultant risk can be expressed as a probability distribution rather than a single isolated point estimate (Frey and Rhodes, 1998; Hattis and Burmaster, 1994; Thompson et al., 1992; U.S.EPA, 2001a).

The principal advantage of the Monte Carlo method is its very general applicability. There is no restriction on the form of the input distributions or the nature of the relationship between input and output, computations are also straightforward. However, there are some disadvantages as well as inconveniences. The exposure assessor should only consider using this technique when there are credible distribution data or ranges for most key variables. Even if these distributions are known, it may not be necessary to apply this technique. For example, if only average exposure values are needed, these can often be computed as accurately by using average values for each of the input parameters. Another inconvenience is that the sensitivity of the results to the input distributions is somewhat complicated to

assess. Changing the distribution of only one value requires rerunning the entire calculation. Finally, Monte Carlo results do not tell the assessor which variables are the most important contributors to output uncertainty. This is a disadvantage since most analyses of uncertainty are performed to find effective ways to reduce uncertainty.

2.6.5 Risk characterization

Risk characterization is the final step of the health risk assessment process. In this step, the information developed through the exposure assessment is combined with CSF and RfD to quantify the cancer risk and noncancer health impacts, respectively. Risk can be characterized according to several types of risk description. They are based on the exposure distribution within the population of interest including individual or population risk, general or susceptible population, point or risk distribution estimate. Risk assessment can be quantitative or qualitative and both are important in different circumstances. Quantitative risk assessment (QRA) is characterized by assigning a numerical value to the risk, in contrast with qualitative risk analysis that is typified by risk ranking or separation into descriptive categories of risk. Several methods can be used to obtain a numerical value for the risk includes point estimates or deterministic QRA and probabilistic QRA (Graham et al., 1992; Richardson, 1996; U.S.EPA, 1995, 2000b; Williams and Paustenbach, 2002).

Risk characterization of noncarcinogenic effects is evaluated by comparing an exposure level (ADD) with toxicity values (RfD). This ratio is called hazard quotient (HQ). To characterize potential carcinogenic effects, probabilities that an individual will develop cancer over a lifetime of exposure are estimated from projected intakes (LADD) and chemical specific dose-response information (CSF). This information is presented in different ways for cancer and noncancer health effects as explained below.

Estimate of noncancer risk is based on the assumption that there is a level of exposure below which it is unlikely to experience adverse health effects. U.S.EPA does not at the present time use a probabilistic approach to estimating the potential for noncarcinogenic health effects. HQ is estimated using the following equation:

$$HQ = \frac{ADD}{RfD} \qquad \text{(Eq.2.4)}$$

where:

HQ = hazard quotient, a unitless = 1

ADD = average daily dose (mg/kg/d)

RfD = reference dose (mg/kg/d)

From the results, if HQ ≤ 1 indicate that exposure are unlikely to result in any adverse health effect, while HQ > 1 suggest that there may be concern for noncancer effects. Risks from simultaneous exposure to more than on chemical or from multiple exposure pathways are generally assumed to be additive. These effects can be evaluated by summing the individual estimated of HQ. To assess the overall potential for noncarcinogenic effects posed by more than one chemical or route, a hazard index (HI) approach has been developed. HI is equal to the sum of the hazard quotients as described in below:

$$\text{Hazard Index} = HQ_1 + HQ_2 + \ldots + HQ_i \qquad \text{(Eq. 2.5)}$$

where:

HQ_i = hazard quotients for the i^{th} toxicant or route

Cancer risk estimation is based on the assumption that the dose-response relationship is linear at low doses. Under this assumption, the slope factor is a constant, and risk will be directly related to intake. The cancer risk equation described in equation below:

$$CR = LADD \times CSF \qquad \text{(Eq. 2.6)}$$

where:

CR = cancer risk, a unitless probability e.g., 1×10^{-4} of an individual developing cancer

LADD = lifetime average daily dose (mg/kg/d)

CSF = cancer slope factor, per (mg/kg/d)

For multiple substances or routes, the equation describes in below:

$$TCR = CR_1 + CR_2 + \ldots + CR_i \qquad \text{(Eq. 2.7)}$$

where:

TCR = the total cancer risk, expressed as a unitless probability

CR_i = the cancer risk estimate for the i^{th} substances or routes.

CHAPTER III

SOIL INGESTION IN THAI PEOPLE

3.1 Introduction

Both children and adults may be exposed to chemicals through indirect pathway. Chemicals can deposit on soil and pose a risk through incidental ingestion of contaminated surface soil. Soil or dust may be ingested by children and adults as a result of normal mouthing behaviors. Generally, children ingest more soil than adults because the hand to mouth activity and behavior patterns. Soil ingestion exposure may be assessed using soil residue data and soil ingestion rates for various age groups. Incidental soil ingestion may be associated with activities such as children playing on areas or adults performing gardening activities or objects including food and cigarettes which have contaminated soil on them.

Estimation of soil ingestion is an important issue in the risk assessment process. The estimation of soil ingestion rates can be performed in two methods. The first method conducts by measure of the soil present on hands and making exposed based on observation of hand to mouth activity. Result of the study is the large uncertainty due to their subjective nature. The second method involves measuring the presence of non-metabolized tracer elements in the feces and soil with a subject is in contact, this method is called a mass balance study (Calabrese et al., 1989; Davis et al., 1990).

The mass balance approach has been used to estimate the amounts of soil ingestion in children and adults. The study is primarily based on tracer elements which present in soil but present in relatively small amounts in foods and poorly absorbed from the gastrointestinal tract. Several tracer elements have been used in the mass balance study including aluminum (Al), cerium (Ce), lanthanum (La),

neodymium (Nd), silicon (Si), titanium (Ti), yttrium (Y), and zirconium (Zr). This study was designed to estimate the amount of soil ingested by Thai adults and children using the mass balance approach with Al, Si, and Y as tracer elements. Al, Si, and Y were selected as tracer elements in this study for two reasons. First, among the eight tracer elements mentioned above, Al, Si, and Y have been shown to be the most reliable tracer elements in the adult validation study of the mass-balance approach with recoveries of approximately 100% and lowest standard deviation of recovery. The investigators concluded that Al, Si and Y are the most reliable tracers for soil ingestion (Calabrese et al., 1989; CalEPA, 2000). Second, since the size of soil particle size ingested by subjected is not known, the tracer elements in soil used to estimate soil ingestion should have relatively homogeneous concentration distributions across the particle sizes. Al, Si, Y have been shown to have relatively homogeneous distribution in the 2 mm and 250 μm particle size diameters (Calabrese and Stanek, 1991; Calabrese et al., 1996; Stanek et al., 1999). The simplified mass balance equation adapted from Stanek and Calabrese (1991) is given by:

$$Ifo + Is = Of + Ou \qquad \text{(Eq. 3.1)}$$

where:

Ifo = amount of tracer element from eating meals (food + water)

= Fo x Fm

= (meals concentration, mg/g)x(amount of meals ingested, g)

Is = amount of tracer element from soil

= Sc x Sa

= (soil concentration, mg/g) x (amount of soil ingested, g)

Of = amount of tracer element from feces

= Fc x Ff

= (fecal concentration, mg/g) x (amount of feces, g)

Ou = amount of tracer element from urine; dried weights

= Uc x Ua

= (urine concentration, mg/g) x (amount of urine, g)

Amount of soil ingestion rate equation is:

$$Sa = \frac{[(Of + Ou) - Ifo]}{Sc} \qquad (Eq. 3.2)$$

Only one study of children soil ingestion has been reported in Thailand. Pongkhamsing (2003) studied soil ingestion in ten children by using aluminum and silicon. Mass balance approach was employed to assess daily soil ingestion. Average and the 95th percentile of soil ingestion based on aluminum were 67.81 and 131.51 mg/d, respectively; based on silicon were 65.97 and 119.7 mg/d, respectively.

Several studies have been conducted to estimate the amount of soil ingested by children. Hawley (1985) estimated that the amount ingested by young children during outdoor activity was 250 mg/d. Binder et al. (1986) studied the soil ingestion rates in 65 children (42 males and 23 females) with aged 1 to 3 years. Excreta were collected over a 3 day period and composited samples of soil were obtained from the yards. The samples were analyzed for aluminum, silicon, and titanium. Soil ingestion by each child was estimated by using assumed fecal dry weight of 15 g/d. They found that the mean of ingestion rate was 181 mg/d with ranged of 25 to 1,324, based on the aluminum; 184 mg/d (ranged 31 to 799), based on the silicon; and 1,834 mg/d (ranged 4 to 17,076), based on the titanium. The 95th percentile values for aluminum, silicon, and titanium were 584, 578, and 9,590 mg/d, respectively. Clausing et al. (1987) conducted a soil ingestion study by using aluminum, titanium, and acid-insoluble residue (AIR) contents were determined for fecal samples from children aged 2 to 4 years. Twenty-seven daily fecal samples were obtained over a 5-day period for the 18 children examined. The ranges of soil ingested were 23 to 979 mg/d with a mean of 230 mg/d for aluminum, 48 to 362 mg/d (mean 129 mg/d) for AIR, and 64 to 11,620 mg/d with mean of 1,430 mg/d for titanium.

Daily soil ingestion was evaluated for the eight tracer elements of aluminum, barium, manganese, silicon, titanium, vanadium, yttrium, and zirconium by collecting and analyzing soil and house dust samples, feces, urine, and duplicate food samples in Calabrese et al. (1989) study. A total of 64 children between the ages of 1 and 4 years were included. It was conducted over 8 days and included the use of a mass-balance methodology. They found that aluminum, silicon, and yttrium were the most reliable of the eight tracer elements analyzed. Using the three most reliable tracer elements for calculate the mean soil intake rate, was estimated to be 153 mg/d based on aluminum, 154 mg/d based on silicon, and 85 mg/d based on yttrium. The 95^{th} percentile values were 223 mg/d for aluminum, 276 mg/d for silicon, and 106 mg/d for yttrium. In the studied of Davis et al. (1990), reported that the mean daily soil ingestion estimates were 38.9 mg/d for aluminum, 82.4 mg/d for silicon, and 245.5 mg/d for titanium. Median values were 25 mg/d for aluminum, 59 mg/d for silicon, and 81 mg/d for titanium.

Van Wijnen et al. (1990) reported that the averages of soil ingestion in age from 1 to 5 years were 69 mg/d for day care children and 120 mg/d for camping group. Geometric mean soil intake was estimated to range from 0 to 90 mg/d with the 90^{th} percentile value of 190 mg/d for the daycare group and 30 to 200 mg/d with the 90^{th} percentile value of 300 mg/d for the camping group. Sedman and Mahmood (1994) used the results of two studies (Calabrese et al., 1989; Davis et al., 1990) to determine estimates of average daily and lifetime soil ingestion in young children. They recommended that an average of soil ingestion in young children of 250 mg/d. Based on the 250 mg/d ingestion rate in a 2 year old child, the average daily soil ingestion over a lifetime was estimated of 70 mg/d. Stanek and Calabrese (1995a) estimated of the soil ingestion by fitting lognormal distributions to the overall daily soil ingestion data from Calabrese et al. (1989). They found that, the mean estimates were 122 mg/d for aluminum; 139 mg/d for silicon, 271 mg/d for titanium and 165 mg/d for yttrium. The overall mean estimate from this reanalysis was 179 mg/d. Then, Stanek and Calabrese (1995b) reported that when the Calabrese et al. (1989) and Davis et al. (1990) studies were combined, the average of soil ingestion was 113 mg/d with the 95^{th} percentile of 217 mg/d by using the best tracer method.

Calabrese et al. (1997a) reported that the median soil ingestion was less than 1 mg/d while the upper 95th percentile was 160 mg/d (ranged of 20 to 500 mg/d), when they were studied in 64 children with aged 1-4 years based on eight naturally occurring soil tracers (Al, Si, Ti, Ce, Nd, La, Y, and Zr) and they recognized that some children have been observed to ingest up to 25-60 g soil during a single day. Stanek et al. (2001) reported that the median soil ingestion was 24 mg/, with the 95th percentile soil ingestion estimated as 91 mg/d by using monte carlo assessment. Davis and Mirick (2006) have been reported that mean of ranges ingested soil in children were 37 to 207 mg/d. Estimates of the amount of soil ingested by children are summarized in Table 3.1.

The mean values ranged from 39 mg/d to 271 mg/d, with an average of 138 mg/d for soil ingestion and 193 mg/d for soil and dust ingestion. The upper percentile values ranged from 106 mg/d to 1432 mg/d (Calabrese et al., 1997b). Based on above studies, U.S.EPA (1991a) recommended that value soil ingestion in children (aged 1-6 years) of 200 mg/d. A value viewed approximately the 95th percentile of the distribution of children soil ingestion. This value was selected from Binder et al. (1986) studied and has been supported by Calabrese et al. (1989) and Davis et al. (1990) studied. In 1997, U.S.EPA new recommended of 100 mg/d for children under six years but indicated 200 mg/d could be used a conservative estimated and the recommendation for the upper percentile of soil ingestion rate was 400 mg/d. For children 7 to 18 years and for adults used 100 mg/d as a soil ingestion rate. However, in 1997 update U.S.EPA indicated that 50 mg/d was still a reasonable estimate for adults (U.S.EPA, 1997a).

Table 3.1 Summary of estimates of soil ingestion by children using Al, Si, and Y

Soil ingestion (mg/d)						References
Mean			Upper percentile			
Al	Si	Y	Al	Si	Y	
181	184	-	584	578	-	Binder et al. (1986)
230	-	-	-	-	-	Clausing et al. (1987)
39	82	-	-	-	-	Davis et al. (1990)
153	154	85	223	276	106	Calabrese et al. (1989)
122	139	165	254	224	144	Stanek and Calabrese (1995a)
133	-	-	217	-	-	Stanek and Calabrese (1995b)
69–120	-	-	-	-	-	Van Wijnen et al. (1990)
66	-	-	280	-	-	Calabrese et al. (1997a)
67.81	65.97	-	131.5	119.7	-	Pongkhamsing (2003)
36.7	38.1	-	107.9	95	-	Davis and Mirick (2006)

In adults data, two adult soil ingestion studies in Thailand have published. Khaokham (2003) studied of the soil ingestion rate in ten adults who live in Pathumthanee province using aluminum and yttrium as trace elements. The mean, the 75^{th} percentile and 95^{th} percentile of soil ingestion based on aluminum were 79.1, 117.0 and 181.7 mg/d, respectively; based on yttrium were 60.3, 96.4 and 188.8 mg/d, respectively. Similarity, Thermphonboon (2003) study showed that the average of soil ingestion were 97.92 and 107.15 mg/d with the 95^{th} percentile of 185.59 and 213.37 mg/d based on aluminum in other group and farmer group, respectively. While average of soil ingestion and the 95^{th} percentile based on yttrium were 45.73 and

49.15 mg/d in farmer group and 144.62 and 178.26 mg/d in other occupations, respectively.

Soil ingestion in adult is limited number of studies. Calabrese et al. (1990) studied six adults to evaluate the soil ingestion rate using ingested of sterilized soil within a gelatin capsule. The ranges of ingestion rate were 30 to 100 mg/d. Stanek and Calabrese (1995b) recalculated ingestion rates that were estimated in Calabrese et al. (1990) for adult soil ingestion. Using the median of the soil ingestion rates based on the best four tracer elements, the adult soil ingestion rates were estimated a mean of 64 mg/d, a median of 87 mg/d and the 90^{th} percentile of 142 mg/d. Soil ingestion in 10 adults estimates with the median, 75^{th} percentile and 95^{th} percentile were 1, 49, and 331 mg/d, respectively that reported by Stanek et al. (1997). Davis and Mirick (2006) reported that a mean soil ingestion rate in adults ranged from 23 to 625 mg/d, depend on the tracer.

U.S.EPA (1997a) uses a soil ingestion rate in adult of 50 mg/d for default value. This rate is based on the study of Stanek et al. (1997). Stanek and his coworkers recommended that U.S.EPA uses the 75^{th} percentile value which was 49 mg/d, as a basic for soil ingestion rate of 50 mg/d for adults. Table 3.2 summarizes the standard of soil ingestion rates in both children and adults.

Table 3.2 Summary of recommended values for soil ingestion by U.S.EPA (1997a)

Population	Soil ingestion (mg/d)	
	Mean	Upper percentile
children	100	400
adults	50	-

This Chapter was conducted to estimate the amount of the ingested soil by Thai children and adults based on trace elements of aluminum, silicon, and yttrium by using a mass-balance approach.

3.2 Materials and Methods

3.2.1 Subjects

Ten healthy adult subjects, five males and five females in the age ranged 25 to 45 years participated in this study. They lived in Pattalung province, a short distance from Ronphibun district and all of them were farmers who worked in the rice paddy or orchards for 6 – 10 hrs per day. The study was conducted over 7 days and included the use of a mass-balance methodology which in addition to soil and dust samples were collected from home and from the places most used by the participants, duplicate samples of food, beverages, medicines, and vitamins were collected and analyzed on a daily basis. Fecal and urine samples were collected and analyzed for tracer elements (Al, Si, and Y).

The children subjects were selected based on families expressed a willingness to participate in the study. A total of 10 children between the ages of 1 and 6 years were included and all of them lived in Pattalung province. Families were required to participate for 7 consecutive days. Parents collected a duplicate food samples, beverages, and medicines the child consumed for 7 consecutive days and collected all feces and some urine excreted. Each participant received compensation for completing the study. Samples were collected in 2005.

3.2.2 Sample collection and preparation

3.2.2.1 Duplicate meal

For both children and adults subjects; duplicate food samples, beverages, and medicines the subject consumed, of each subject were collected from the breakfast of day 1 through the evening meal of day 7. Duplicate foods were collected for 7 consecutive days for each participant. Food samples were pooled on each day, weighed, and frozen until analysis. A homogenized food sample of 10 g was weighed in duplicate into 100 ml digestion beaker, added concentration of perchloric acid : nitric acid (1:10) as 50 ml and allowed to stand overnight. The beakers were then heated on hot plate until the dense white fumes of an acid was occurred. After cooling, diluted in deionized water and made up to 50 ml and then filtered through a Whatman no. 42 filter paper. The solution was transferred into a volumetric flask and adjusted to the volume with 5% nitric acid.

3.2.2.2 Fecal samples

Fecal samples were collected from noon of day 2 through midnight of day 8. Total fecal samples were pooled on each day, air-dried (95 ºC), weighed, and frozen until analysis. A 5 g of homogenized fecal sample was accurately weighed, placed in beaker (two replicates for each sample) and digested with perchloric acid and nitric acid (1:10) solution with 50 ml for 15-18 hrs. Then, sample was heated by hot plate. Heating was stopped when the dense white fumes of an acid occurred. The digests were cooled, diluted in 50 ml distilled deionized water and filtered into volumetric flask through filter paper (Whatman, No. 42). The solution sample was adjusted to the volume with 5% nitric acid.

3.2.2.3 Urine samples

All subjects were provided with polyethylene bottles of 2.5 l capacity for their 24 hrs urine collection. Urine samples were collected from noon of day 1 through midnight of day 7. Precautions were taken to avoid any possible contact between collection bottles and urine samples. At the end of each collection on each day, the urine samples were pooled and frozen until further analysis. The 0.5 g aliquots urine sample was prepared for tracer elements analysis by the same procedure of fecal samples preparation. The concentrations of tracer elements in urine samples were estimated in mg of dried-weights. In the study, amount of urine was not reported because it was embedded in the expression used for amount of each tracer element in urine, already.

3.2.2.4 Soil and dust samples

Dust samples were vacuumed from the floor of the room in which subjects spent during the stay awake in the house. All dust samples collected from each subject's home during the study were mixed to produce a single sample, air-dried and sieved. Soil samples were collected from two to four sites in the yards where the subjects spent the most time during the study period. They were collected from the upper 0 - 15 cm of about 100 g from each identified sites, air-dried, thoroughly mixed, and sieved to separate soil from non-soil large materials. Soil and dust samples from each site were mixed together with equal dry weights to produce a single soil sample for each subject. Soil samples were analyzed in aliquots weighing approximately 0.25 g by acid digestion with the same method of duplicate meal sample analyzed.

3.2.3 Reagents

Standard Reference Materials 2709 (San Joaquin Soil) was obtained from the National Institute for Standards and Technology (NIST), USA. Standard solutions of Al, Si, and Y (1,000 μg/ml) were purchased from Merck. Other chemicals were reagent grades.

3.2.4 Analysis of samples

Analyses of tracer elements in samples were performed on an inductively coupled plasma-atomic emission spectrometry (ICP-AES, Perkin Elmer Plasma II). The working conditions are described below.

Instrumental parameter for ICP-AES	
Frequency (mHz)	27.12
Incident power (kW)	1.0
Argon gas flow rates (l/min)	
Outer	15
Intermediate	1.0
Nebulizer	0.7
Observation height (mm)	15
Read delay (s)	20
Sampling time (ms)	100
Analytical wavelength (nm)	
Al	396.15
Si	251.61
Y	371.03

3.2.5 Analysis assurance

The accuracy of soil and dust analyses was evaluated by analyzing NIST Standard Reference Materials 2709 (San Joaquin Soil). Standard addition method was used to evaluate the accuracy of analysis for food and fecal samples.

3.2.6 Statistical analysis

The estimation of soil ingestion rate for a given tracer element was as follow Equation 3.2. Student's t-test statistic is used for comparison of tracer elements concentration in duplicate meal, soil, feces, and urine samples between the genders of each group and to compare soil ingestion rate between genders.

3.3 Results

3.3.1 Accuracy of the analysis

The average recoveries of Al, Si, and Y in the SRM 2709 (San Joaquin Soil) were 93.9, 94.7 and 92.3% (n = 10). The mean recoveries in the spiked food were 94.7, 95.3 and 92.1%, respectively (n = 10). The average recoveries of Al, Si, and Y in spiked fecal samples were 95.8, 95.9 and 93.4% (n = 10).

3.3.2 Concentrations of Al, Si, and Y in soil and dust samples

Concentrations of Al, Si, and Y in soil and dust samples are summarized in Table 3.3. In adults study, the ranges of tracer elements concentration were 0.07 to 0.081 mg/g for Al, 0.292 to 0.36 mg/g for Si, and 16.32 to 18.83 µg/g for Y. The average concentration of Al, Si, and Y were 0.076 mg/g, 0.33 mg/g, and 17.596 µg/g for adults, respectively. In children, the mean of Al, Si, and Y in soil samples were 0.073 mg/g (ranged 0.068 to 0.078 mg/g), 0.29 mg/g (ranged 0.269 to 0.304 mg/g), and 17.594 µg/g (ranged 16.09 to 19.15 µg/g), respectively.

Table 3.3 Concentration of Al, Si, and Y in soil and dust samples

Statistical value	Al (mg/g)		Si (mg/g)		Y (μg/g)	
	Adults	Children	Adults	Children	Adults	Children
Min	0.07	0.038	0.292	0.269	16.32	16.09
Mean	0.076	0.073	0.33	0.29	17.596	17.594
SD	0.003	0.003	0.02	0.29	1.01	0.93
5^{th} percentile	0.07	0.068	0.292	0.269	16.32	16.09
25^{th} percentile	0.073	0.071	0.32	0.286	16.61	16.97
Median	0.076	0.073	0.33	0.296	17.61	17.65
75^{th} percentile	0.078	0.075	0.35	0.303	18.67	18.02
90^{th} percentile	0.08	0.077	0.358	0.303	18.785	18.97
95^{th} percentile	0.081	0.078	0.36	0.304	18.83	19.15
Max	0.081	0.078	0.36	0.304	18.83	19.15

3.3.3 Food ingestion and feces excretion

Daily freeze-dried weights of food samples and fecal samples are presented in Table 3.4. Daily dried weights of food samples ranged from 199.4 to 407.8 g with the mean value of 301.91g for adults group, while daily dried weights of food samples ranged from 150.3 to 376.7 g with the mean value of 232.81 g for children group.

Daily fecal freeze-dried weights varied from 11.05 to 35.03 g with the mean weight of 18.94 g for adults group and daily dried weights of fecal samples ranged from 7.55 to 21.53 g with the mean value of 12.96 g for children group. Of the 70 subject-days, there were 44 subject-days with one fecal sample per day, 22 subject-days with two fecal samples per day, and 4 subject-days with three fecal samples per day.

Table 3.4 Daily freeze-dried weight of meal and fecal samples

Statistical value	Food (g)		Feces (g)	
	Adults	Children	Adults	Children
Min	199.4	150.3	11.05	7.55
Mean	301.91	232.81	18.94	12.96
SD	48.79	50.27	4.75	3.06
5^{th} percentile	229.6	171.5	12.64	8.59
25^{th} percentile	266.7	194.5	15.56	10.93
Median	304.35	223.1	18.38	12.66
75^{th} percentile	326.8	261.7	20.94	14.36
90^{th} percentile	371.95	311.45	25.17	17.24
95^{th} percentile	381.4	332.6	28.91	19.44
Max	407.8	376.7	35.03	21.53

Table 3.5 summarizes the total amounts of Al, Si, and Y in duplicate meal and the daily amounts excreted in feces and urine for adults. The ranges of total tracer element consumption from food were 2.14 to 5.88 mg for Al, 5.78 to 43.09 mg for Si, and 1.02 to 3.54 µg for Y. Total amounts of Al excreted in feces ranged from 1.24 to 21.01 mg. The ranges for Si and Y concentration in feces were 13.01 to 112.27 mg and 0.86 to 7.17 µg, respectively. The ranges of tracer elements from urine were 0.007 to 0.06 mg for Al, 0.23 to 4.15 mg for Si, and 0 to 0.089 µg for Y.

Table 3.5 Daily amounts of Al, Si, and Y in food, fecal, and urine samples of adults

Statistical value	Food			Feces			Urine		
	Al (mg)	Si (mg)	Y (µg)	Al (mg)	Si (mg)	Y (µg)	Al (mg)	Si (mg)	Y (µg)
Min	2.14	5.78	1.02	1.24	13.01	0.86	0.007	0.23	0
Mean	3.56	26.22	1.91	5.61	32.67	2.29	0.023	1.22	0.035
SD	0.87	5.98	0.55	3.36	16.58	1.18	0.012	0.71	0.03
5^{th} percentile	2.45	18.98	1.11	2.35	15.73	1	0.007	0.37	0
25^{th} percentile	2.96	22.57	1.5	4.07	2176	1.48	0.014	0.74	0
Median	3.35	25.47	1.86	4.73	28.27	2.02	0.021	1.15	0.042
75^{th} percentile	4.08	29.55	2.24	6.58	40.3	2.66	0.031	1.45	0.062
90^{th} percentile	5.04	33.18	2.76	8.45	48.3	3.75	0.04	1.94	0.072
95^{th} percentile	5.32	36.19	2.9	11.73	69.96	4.55	0.043	2.55	0.08
Max	5.88	43.09	3.54	21.01	112.27	7.17	0.06	4.15	0.089

Table 3.6 presents the averages of total tracer elements consumption by children from food were 2.54 mg with ranged of 1.24 to 4.8 mg for Al, 19.29 mg (ranged 9.76 to 32.33 mg) for Si, and 1.33 µg (ranged 0.65 to 2.41 µg) for Y. Total amounts of Al excreted in feces ranged from 1.03 to 21.87 mg. The ranges for Si and Y concentration in feces were 7.63 to 74.82 mg and 0.61 to 6.07 µg, respectively. The ranges of tracer elements from urine were 0.004 to 0.04 mg for Al, 0.3 to 3.25 mg for Si, and 0 to 0.095 µg for Y.

Table 3.6 Daily amounts of Al, Si, and Y in food, fecal, and urine samples of children

Statistical value	Food			Feces			Urine		
	Al (mg)	Si (mg)	Y (µg)	Al (mg)	Si (mg)	Y (µg)	Al (mg)	Si (mg)	Y (µg)
Min	1.24	9.76	0.65	1.03	7.63	0.61	0.004	0.3	0
Mean	2.54	19.29	1.33	4.72	27.07	1.82	0.017	1.05	0.027
SD	0.73	5.70	0.38	4.42	15.12	1.04	0.008	0.65	0.03
5^{th} percentile	1.48	11.06	0.72	1.32	10.78	0.72	0.007	0.34	0
25^{th} percentile	2.08	13.52	1.1	2.19	17.21	1.12	0.011	0.55	0
Median	2.36	13.38	1.26	3.19	22.39	1.46	0.015	0.89	0.015
75^{th} percentile	2.99	23.58	1.54	5.93	31.82	2.29	0.022	1.49	0.044
90^{th} percentile	3.69	26.99	1.86	9.47	48.32	3.03	0.027	1.95	0.082
95^{th} percentile	3.84	29.3	2.02	16.03	56.95	4.06	0.029	2.22	0.091
Max	4.8	32.33	2.41	21.87	74.82	6.07	0.04	3.25	0.095

3.3.4 Soil ingestion rates

Statistical distributions of daily soil ingestion estimates in adults are shown in Table 3.7. Mean daily soil ingestion estimates were 27.16 mg/d for Al, 22.53 mg/d for Si, and 23.47 mg/d for Y. The median estimates were 19.14 mg/d (Al), 8.85 mg/d (Si), and 9.68 mg/d (Y). The 95^{th} percentile values based on Al, Si, and Y were 106.7, 127.39, and 114.77 mg/d, respectively.

Table 3.7 Estimation of daily soil ingestion in adults

Statistical value	Al (mg/d)	Si (mg/d)	Y (mg/d)
Min	-22.78	-36.52	-53.59
Mean	27.16	22.53	23.47
SD	41.38	44.92	57.45
5^{th} percentile	-12.5	-26.78	-43.51
25^{th} percentile	1.38	-3.58	-13.69
Median	19.14	8.85	9.68
75^{th} percentile	40.57	33.36	36.93
90^{th} percentile	68.15	87.82	80.3
95^{th} percentile	106.7	127.39	114.77
Max	194.96	198.25	255.91

The estimation of soil ingestion rates in children are shown in Table 3.8. The averages of soil ingestion were 29.88 mg/d with the 95^{th} percentile of 190.94 mg/d, based on Al; 36.33 mg/d (the 95^{th} percentile of 173.35 mg/d), based on Si; and 30.05 mg/d (the 95^{th} percentile of 299.37), based on Y.

3.3.5 Statistics analysis

Student's t-test statistics is used for comparing concentration of each tracer elements in all samples between genders of children and adult group. The p-value results are summarized in Table 3.9. In adults, concentration of all tracer elements in all samples and soil ingestion rate were not significantly different between the genders except Y in soil ($p < 0.05$), food and fecal weights ($p< 0.05$) that found in male more than female. While in children, all tracer elements in food, urine and Y in soil samples

from male were significantly higher ($p < 0.05$) than female including fecal and food weights ($p < 0.01$) but soil ingestion rates were not different between the genders.

Table 3.8 Estimation of daily soil ingestion in children

Statistical value	Al (mg/d)	Si (mg/d)	Y (mg/d)
Min	-20.61	-39.8	-35.63
Mean	29.88	36.33	30.05
SD	61.68	57.74	58.23
5^{th} percentile	-16.93	-24.48	-30.27
25^{th} percentile	-2.01	0.58	-5.58
Median	10.91	22.95	11.28
75^{th} percentile	37.74	60.71	53.03
90^{th} percentile	84.29	87.55	84.18
95^{th} percentile	190.94	173.35	157.38
Max	283.7	256.11	299.37

Table 3.9 Results of comparison of concentration tracer elements between genders

Variables	Tracer element	Adults (p-value)	Children (p-value)
Food concentration	Al	0.51	< 0.01
	Si	0.26	< 0.01
	Y	0.24	< 0.01
Fecal concentration	Al	0.16	0.83
	Si	0.28	0.86
	Y	0.87	0.9
Urine concentration	Al	0.21	< 0.01
	Si	0.17	< 0.01
	Y	0.19	< 0.05
Food weights	-	< 0.01	< 0.01
Fecal weights	-	< 0.01	< 0.01
Soil ingestion rate	Al	0.45	0.76
	Si	0.41	0.12
	Y	0.78	0.51
Soil concentration	Al	0.41	0.83
	Si	0.51	0.63
	Y	< 0.05	< 0.05

3.4 Discussion

The mass balance approach can produce negative soil ingestion estimates which are an artifact of the method. This artifact is a result of food intake and fecal output misalignment. An input-output misalignment could result in under- or overestimation of soil ingestion. Subjects who consumed relatively high amounts of tracer elements from food on the day before or during the study period would excrete high concentrations of the tracers in their feces over the next few days which could result in overestimation of soil ingestion. On the other hand, consumption of relatively low level of tracer elements would result in underestimation of soil ingestion. Underestimation is illustrated by negative values of soil ingestion. The study over 7 consecutive days could minimize the misalignment error (Calabrese et al., 1997). Of the 70 soil ingestion estimates for each tracer obtained in the adults group, all three tracers had negative soil ingestion estimates of 20 to 34% (20% for Al, 28.5% for Si, and 34 for Y in adult samples; 28.5% for Al , 23% for Si, and 27% for Y in children group). Davis et al. (1990) reported that the calculated quantities for soil ingestion were negative value for 13 to 32%. This provides some indication of the degree to which input and output mismatch occurred.

However, the mass-balance studies of soil ingestion have an advantage over other indirect approaches because it has been validated by Calabrese et al. (1990) and Stanek et al. (1997) studied. Generally assumptions in the mass-balance approach are assumed that any soil ingested is from the subject's yard and the tracer elements concentration is uniform throughout the yard. Then, it is assumed that the tracer elements are minimally absorbed. The absorption of aluminum was estimated of 0.1%. Si and Y may be were higher absorbed than aluminum but there were no comparable data for them (Davis, 1990). The degree of absorption occurs cannot be determined from the present study. However, the results in Table 3.5-3.6 would suggested that silicon may be absorbed to a greater degree than aluminum and yttrium. A limitation of the methodology and results are same the previous studies

briefly for each subject and day, a nonrandom sampling of subjects, a limited period of study, and based on many assumptions (Simon, 1998).

The present study provides soil ingestion estimates with 10 adults and 10 children subjects using Al, Si, and Y as tracer based mass-balance study over 7 days of study. The completeness results of duplicate meal, excreta, soil and dust samples are presented in Table 3.3-3.6 and Table 3.7 and 3.8 presents the results of soil ingestion rate in Thai adults and children.

Table 3.10 summarizes of soil ingestion rate from the present study in both adults and children. Soil ingestion rate for children in the present study are within the ranges of estimates reported by previous studies (Binder et al., 1986; Clausing et al., 1987; Calabrese et al., 1989; Calabrese et al. 1997a,b; David and Mirick, 2006; Davis et al., 1990; Stanek and Calabrese, 1995; Stanek and Calabrese, 2000; Pongkhamsing, 2003; van Wijnen et al., 1990). However, the results from the present study were lower than those of previous studies. These effects are described on the difference of many factors such as tracer elements concentration in soil, food or nonfood, types of food, pattern of activities, hand to mouth activity, and geographical regions.

From U.S.EPA (1997a, 2006) handbooks indicates 100 mg/d as the mean and 400 mg/d as the upper 95^{th} percentile for children. The handbooks recommendations are not the default values for use in risk assessment, default values are set for the Superfund program in Risk Assessment Guidance for Superfund uses of 200 mg/d soil ingestion for children for reasonable maximum exposure. ATSDR's Public Health Assessment Guidance Manual also recommends the use of 200 mg/d for soil exposure estimation for children (ATSRD, 2005b). This value is similar to the present study with the ranged of the 95^{th} percentile as 157 to 190 mg/d. U.S.EPA suggested that risk assessor should use the soil ingestion rate by regional studied if possible, because soil ingestion may be an important factor in the characterization of adverse effects in area especially contaminated sites.

Table 3.10 Summary of soil ingestion estimates in the present study

Participant	Tracer element	Soil ingestion rate				
		Mean	Median	75^{th} percentile	90^{th} percentile	95^{th} percentile
Children	Al	29.88	10.91	37.74	84.29	190.94
	Si	36.33	22.95	60.71	87.55	173.35
	Y	30.05	11.28	53.03	84.18	157.38
Adult	Al	27.16	19.14	40.57	68.15	106.7
	Si	22.53	8.85	33.36	87.82	127.39
	Y	23.47	9.68	36.93	80.3	114.77

Tracer elements intake and excrete vary day by day depending on the concentration in food and soil, consumption patterns, and activities of each subject. Soil ingestion rates are more variable in children than in adult. Table 3.11-3.13 compare the results of soil ingestion study form the present study with other studies. Variation from day to day may result in inducing variability in daily soil ingestion estimates. However, there are currently no data to support the variability in a day or in each tracer element reflects variability over daily soil ingestion rate.

Table 3.11 Comparison of soil ingestion in children by Al, Si, and Y (mg/d)

Statistical value	Al (mg/d)	Si (mg/d)	Y (mg/d)	References
Mean	1	-19	38	Calabrese et al. (1996)
	37	38	-	David and Mirick (2006)
	30	36	30	Present study
SD	90	64	116	Calabrese et al. (1996)
	35	31	-	David and Mirick (2006)
	62	58	58	Present study
Min	-201	-147	-493	Calabrese et al. (1996)
	-21	-40	-36	Present study
Median	-3	-22	28	Calabrese et al. (1996)
	33	26	-	David and Mirick (2006)
	11	23	11	Present study
90^{th} percentile	52	39	209	Calabrese et al. (1996)
	84	88	84	Present study
95^{th} percentile	97	87	220	Calabrese et al. (1996)
	191	173	299	Present study
Max	403	288	270	Calabrese et al. (1996)
	108	95	-	David and Mirick (2006)
	284	256	299	Present study

Table 3.12 Soil ingestion estimates in each day of children studies (mg/d)

Tracer element	Days							References*
	1	2	3	4	5	6	7	
Al	5	34	5	5	-215	50	722	1
	5.88	-1.9	28.8	40.3	46.6	21.2	68	2
Si	21	-7	-4	-4	68	79	702	1
	18.69	9.7	67.5	53.5	27.6	45.7	32	2
Y	94	113	74	74	228	177	780	1
	24.9	13.8	22.8	23.3	15.9	23.8	89	2

(*) [1]Stanek and Calabrese (2000); [2] present study

In adults, the results of soil ingestion rate in the present study are in agreement with Calabrese et al. (1990), David and Mirick (2006), Khaokham (2003), Stanek and Calabrese (1995), Stanek et al. (1997), and Thermphonnboon (2003) studied as well as federal guideline which suggest of 50 mg/d (U.S.EPA, 1997a). A comparable of the distribution of soil ingestion rates among the adult studies are showed in Table 3.13. Many reasons for the difference rate of ingestion for example seasonal effects. Almost of soil ingestion studies were conducted experimental in summer months. Therefore, daily amount soil ingestion estimates were larger than the distribution of soil ingestion estimates reported in other seasons. Currently, there are no available estimates of seasonal effects on soil ingestion.

Table 3.13 Comparison of mean and median of soil ingestion estimates in adults based on tracer elements (mg/d)

No. of subjects	Subject-days	Al		Si		Y		References*
		Mean	Median	Mean	Median	Mean	Median	
10	70	12	5	-20	-24	187	-40	1
6	54	77	57	5	1	53	65	2
19	19	92.1	0	23.2	5.2	-	-	3
		68.4	23.2	26.1	0.2	-	-	3
10	70	79.1	-	-	-	60.3	-	4
10	70	97.9	-	-	-	45.7	-	5
10	70	27	19	23	9	23	10	6

*[1]Stanek et al. (1997), data presented in the table are from the first week of the studies, [2]Calabrese et al. (1990), [3]David and Mirick (2006), data presented in the row above is from mother samples and other below is from father samples, [4]Khaokham (2003), [5]Thermphonnboon (2003), [6] Present study

In both adults and children, soil ingestions were varied by day to day, inter-individuals and among tracer elements. However, in this study were not significantly different soil ingestion rates ($p \geq 0.12$) between male and female both adults and children group and not significantly different of tracer elements concentration in soil samples but the concentration of all trace elements in food, feces, and urine were significantly different ($p < 0.01$) between male and female in children. May be, these results were due to high ingesting rate of contaminant meals of them and his activity patterns. In adults, amounts of tracer elements in meal, feces, and urine were not different in concentrations.

Tracer elements concentrations in duplicate meal samples were different between boy and girl may be resulted from the difference type of food and pattern of

consumption. Generally, a boy consumed food or everything more than girl in this ages and tried everything that possible ingested. Normally, tracer elements were excreted by urine in a few amounts. From the present study, all elements were excreted by urine ≤ 4% of total excretion (feces plus urine) both adult and children group. The difference of tracer elements in urine samples between the genders in children group has effect of zero value about 48.5% of total samples on the calculation.

U.S.EPA recommended that 50 mg/d for a mean and may be used of 100 mg/d for the upper percentile of soil ingestion rate in adults. The mean of soil ingestion rate was of 50 mg/d came from the 75^{th} percentile value, thus it was higher than the actual mean of soil ingestion rate in the present study. However, the 95^{th} percentile value from Stanek et al. (1997) was 331 mg/d but U.S.EPA selected of 100 mg/d for the upper percentile rate of soil ingestion, based on the expert judgments (U.S.EPA, 1997a). From Table 3.10, comparison of soil ingestion estimates in each rate, in Thai people should use the ranges of 75^{th} percentile for a mean of soil ingestion rate (the same value of Stanek et al. (1997) suggested to U.S.EPA) in both adults and children, because the present results had negative soil ingestion estimates approximately 25% (Figure 3.1 and 3.2). This average ingestion rate was extended over at least 50% of participants. Thus, the recommendation is used that 35 mg/d (ranged of 33.36 to 40.57 mg/d based on three tracer elements) and 120 mg/d (ranged 106.7 to 127.39 mg/d) for a mean and the upper percentile, respectively for Thai adults. The mean (35 mg/d) of soil ingestion rate approximately 75% of adults were included. While, 95% of adults covered with 120 mg/d of ingestion rate. Only 5% of adults ingested soil > 120 mg/d. Comparison of soil ingestion rates from the present study with U.S.EPA standard value in adults in percentage of participants are shown in Table 3.14. Figure 3.1 presents the cumulative distribution of soil ingestion based on each tracer elements.

Table 3.14 Comparison of percent of soil ingestion rate from the present study with U.S.EPA standard value in adults

Participant	Soil ingestion rate*					
	≤25 mg/d	≤35 mg/d	≤50 mg/d	≤75 mg/d	≤ 100 mg/d	≤ 120 mg/d
Adult (%)	52	75	80	90	91.5	95

*U.S.EPA recommended that 50 mg/d for a mean of soil ingestion rate.

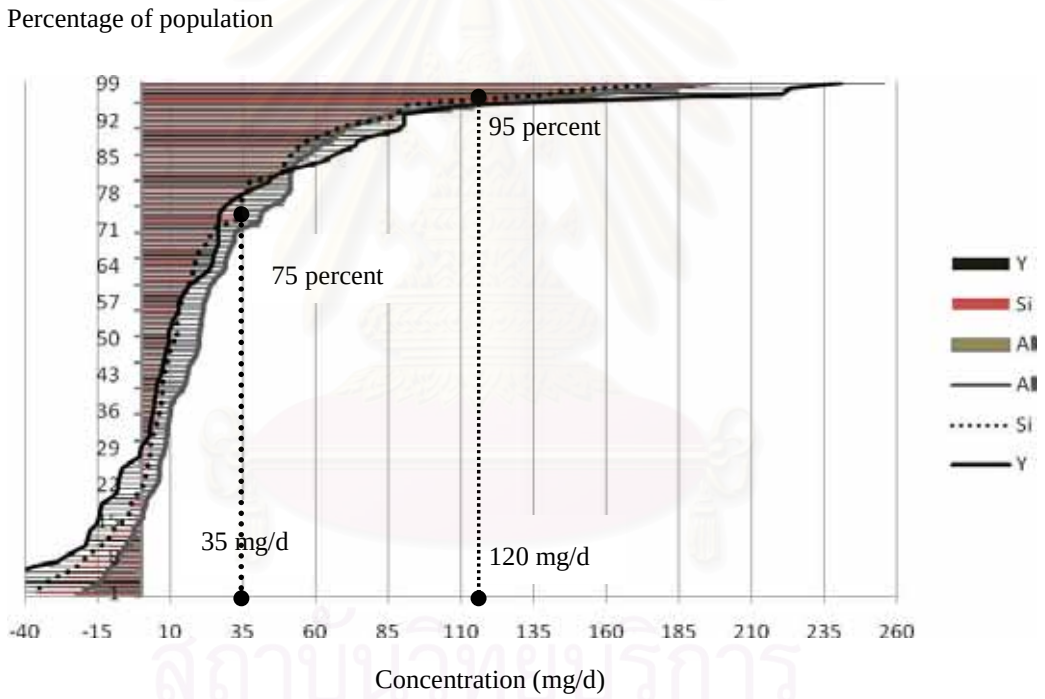


Figure 3.1 Cumulative distribution of soil ingestion rates in Thai adults

In children, 74% of children ingested soil ≤ 50 mg/d with ranged of 37.74 to 60.71 mg/d based on all elements. The upper percentile of soil ingestion rate in children, 96% of ingested soil ≤ 175 mg/d (ranged from 109.94 to 190.94 mg/d). These values were estimated from the 95th percentile of all tracer elements data. Only 4% of children ingested soil more than 175 mg/d. Therefore, the recommendation should be uses 50 mg/d and 175 mg/d for mean and the upper percentile, respectively for soil ingestion rate of Thai children. This average value is extended to

approximately 74% of children. While, 96% of children covered with 175 mg/d of soil ingestion rate. Comparison of soil ingestion rates from the present study with U.S.EPA standard value in children are presented in Table 3.15 and Figure 3.2 shows the cumulative distribution of soil ingestion in children based on each tracer elements.

Table 3.15 Comparison of percent of soil ingestion rate from the present study with U.S.EPA standard value in children

Participant	Soil ingestion rate*					
	≤ 35 mg/d	≤ 50 mg/d	≤ 85 mg/d	≤ 100 mg/d	≤ 175 mg/d	≤ 400 mg/d
Children (%)	70	74	90	92	96	100

*U.S.EPA recommended that 100 mg/d for a mean and 400 mg/d for the upper percentile of soil ingestion rate.

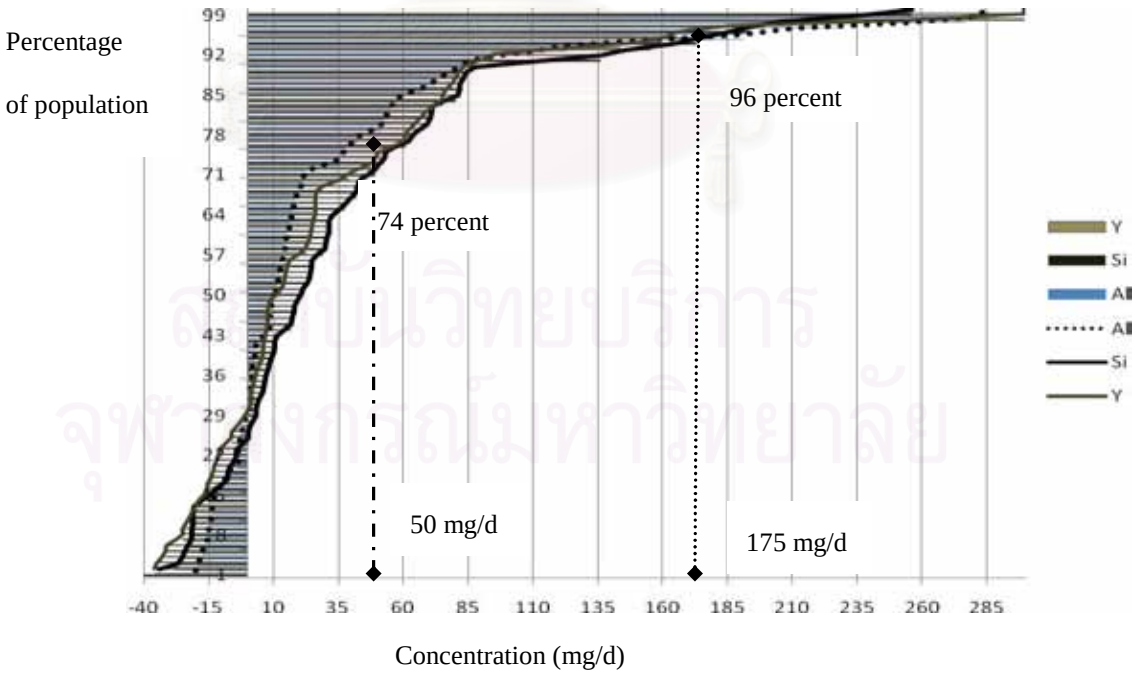


Figure 3.2 Cumulative distribution of soil ingestion rates in Thai children

In conclusion, the values of 35 mg/d for mean and 120 mg/d for the upper percentile of soil ingestion rate was used for Thai adults. The values of 50 mg/d and 175 mg/d for mean and the upper percentile was selected for Thai children to evaluate arsenic risk assessment from ingested soil in Ronphibun's residents in next Chapter. Besides, the benefit of these results are address concerns that exposure and risk assessments lack the knowledge of soil ingestion in Thai people.

CHAPTER IV

MATERIALS AND METHODS

4.1 Study Area and Population

The present study was focused on the 4 villages of Ronphibun subdistrict include villages number 1, 2, 12, and 13 (Figure 4.1). Because almost (>85 %) all the patients that suffered from arsenic chronic have lived in these areas and there were reported that the hot spots for high level of arsenic in soil and water. Ronphibun subdistrict has 16 villages with population more than 20,000 in census records. The data from local provincial office reported that total 11,005 people have been living in this subdistrict and 2,289 people in village number 1, 2, 12 and 13. This study used purposive sampling method for collecting samples from 16 people (8 males and 8 females) for 7 consecutive days and all of them agreed to participate in the study. The study was carried out between October 2006 and December 2007.

4.2 Arsenic Intake from Duplicate Meal Consumption

Exposure to contaminants in food can be assessed as four different types of data: food supply data, household survey data, dietary survey among individual data and duplicate meal data. The duplicate meal approach differs from the other methods because the intake estimation does not depend on composition data from other sources. The concentration is measured by directly contaminant analysis of the duplicate diet (Mohri et al., 1990; Ohno et al., 2007; Tsuda et al., 1995).

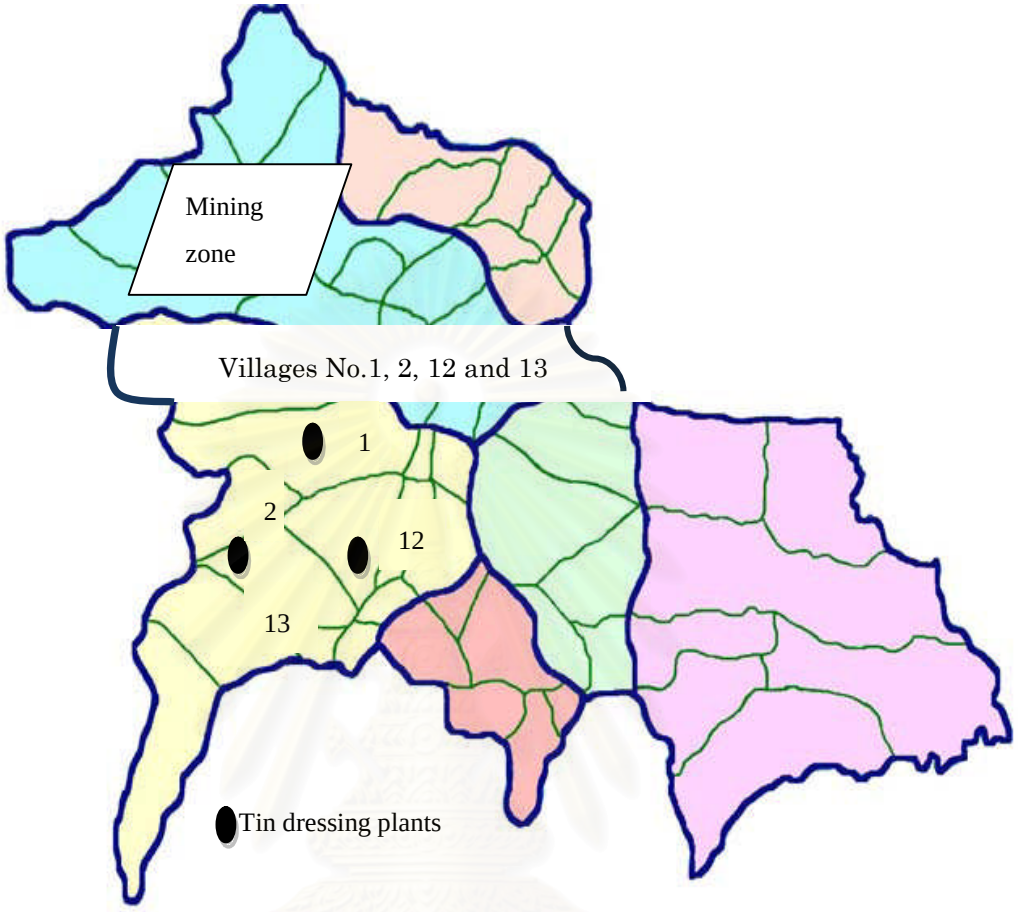


Figure 4.1 Location of study in Ronphibun subdistrict

Cooking methods vary in different countries for example, people cook rice with very little water in Japan whereas in Bangladesh, rice is cooked with excess water and water that is not absorbed during cooking is discarded. Thus, the arsenic concentration may differ from the method of cooking (Bae et al., 2002; Rahman et al., 2006; WHO, 2001). Duplicate portion study designs provide food samples as actually consumed rather than samples of unprepared or individual food items that are typical of surveillance approaches to characterizing dietary exposures (Devesa et al., 2008). The concentration levels measured in duplicate portion samples are likely to more accurately reflect personal dietary ingestion exposures than raw materials and other foods collected at the producer or distributor level. Arsenic contamination of groundwater has been reported from many parts of this area. Recently, many people

try to avoid drinking arsenic contaminated groundwater because they have become aware of the risk of the arsenic contamination; instead, they obtain drinking water from less contaminated sources from bottle water or rainwater. Therefore, the use of arsenic concentrations in contaminated groundwater to indicate drinking water concentrations may lead to overestimation of the recent arsenic intake. Depending on the objective of this study drinking water and all beverages were included as part of the duplicate portion samples.

The aims of this Section study were to investigate the contribution of food and water in term of duplicate meal to the arsenic intake in adults after they obtain the less contaminated drinking water sources and to investigate whether they use uncontaminated water sources not only for drinking but for cooking. To evaluate arsenic intake via food, including via cooking water, a duplicate portion sampling method was used. Children, especially in contaminated area was concerned about adverse effects from exposure to contaminated soil more than other pathways because they can be exposed to contaminants in soil from playing or other activities and higher of soil ingestion rate. Thus, risk assessment in children was only evaluated by ingested soil pathway.

4.2.1 Sample Collection and Preparation

4.2.1.1 Duplicate meal sample

Duplicate food samples, all beverages (e.g., drinking water, coffee, tea), and other materials (e.g., vitamin, drug) consumption were collected by the duplicate portion sampling method (Tsuda et al., 1995). Each participant submitted daily duplicate meal samples for 7 day. A hundred and twelve samples of duplicate meal were collected for seven consecutive days from all participants (n=112 subject-days). Volunteers were asked to collect an exact duplicate of food, beverages and medicine they have ate and drank during the 7 days study. Participants received compensation before duplicate food sample and participant in the project. Meal

samples were collected and placed in plastic bags that were sealed and then placed and sealed in a second plastic bag. Each meal was collected in a separate plastic bag. Participants ingested something throughout a day, they stored an equivalent sample in a plastic bag supplied by the laboratory and wrote on the package the sampling time and the nature of the food. Usually, each person participated three times in the collection of meals. Drinking water and beverages samples were collected from the present drinking water source of each participant in clean bottles. The sample containers were stored in the domestic refrigerator until transportation. After collection phase, the samples were stored in a cold box and transported to the laboratory by train.

In laboratory, inedible parts of the foods were discarded, sliced and mixed all duplicate meals (foods, all beverages and other materials intake) on each day were blended to give homogeneous sample using blender. The sample was weighed, frozen, freeze-dried, and stored in polyethylene bags until analysis. A known amount of the resulting slurry was lyophilized and powered residue was weighed so that the daily intake of arsenic could be estimated. In this study, all beverages intake rate does not report because it was embedded in the expression used for amount of arsenic concentration in duplicate meal sample (mg/g, dry weight), already.

4.2.2 Extraction of Total Arsenic in Duplicate Meal

The lyophilized sample of about 0.2 g was placed into 250 ml beaker. A mixture of nitric and perchloric acid in a ratio 10:1 as 50 ml was added for an overnight digestion. After the digestion, the sample was heated on hot plate until the dense white fumes of an acid was occurred. After cooling, the residue was diluted in distilled water and then filtered through filter paper (Whatman no. 42). Then, the solution was transferred into a volumetric flask and adjusted to the volume with 5% nitric acid. The sample was analyzed for arsenic using hydride generation-atomic absorption spectrometry (HG-AAS).

4.2.3 Extraction of Inorganic Arsenic in Duplicate Meal

An accurate weight (0.5 g) of lyophilized sample was placed in a 50 ml screw-top centrifuge tube. Amount of 4.1 ml deionized water was added and agitated until completely moistened. Then 18.4 ml of concentrated hydrochloric acid was added and agitated for 1 hr, and left to stand for 15-18 hrs (overnight). The reducing agent, 1 ml of 1.5% w/v hydrazine sulfate solution and 2 ml of hydrobromic acid was added and agitate for 30 seconds. Add 10 ml of chloroform and agitate for 3 min. The phases were separated by centrifuging at 1,500 *g* for 5 mins. It was separated the chloroform phase by aspiration and poured it into another tube. The extraction process was repeated two more times. The chloroform phases were combined and centrifuged again. The remnants of the acid phase were eliminated by aspiration. Eliminate possible remnants of organic material in the chloroform phase were eliminated by passing it through filter. Back-extract the inorganic arsenic in the chloroform phase by agitated for 3 mins with 10 ml of 1 mol/l hydrochloric acid. The phases were separated by centrifuging at 1,500 *g*, and the aqueous phase was then aspirated and poured into a beaker, repeated this stage once again and the back-extraction phases obtained. When the back-extraction phase generated emulsions that could not be broken by centrifuging at over 1,500 *g* for 5 mins, the emulsion was transferred to the beaker. Added nitric acid in ashing aid suspension and it was heated on hot plate. The emulsion was then broken and the chloroform phase formed was removed by aspiration. For determine inorganic arsenic in the back-extraction phases were added 2.5 ml of ashing aid suspension and 10 ml of concentrated nitric acid to combined back-extraction phases. Digestion and determination of inorganic arsenic were used the same method as for total arsenic (Huang et al., 2003; Munoz et al., 1999, 2000).

4.2.4 Determination of Arsenic

The amount of arsenic in duplicate meal samples determined by hydride generation atomic-absorption spectrometry (HG-AAS). The operating conditions for the HG-AAS system are listed in below. The instrument detection limits for this system were 0.05 µg/g for total arsenic and 0.02 µg/g for inorganic arsenic.

HG-AAS operating conditions

Carrier gas	N_2
Carrier gas flow rate	200 ml/min
HCl concentration	0.12M
HCl flow rate	6.1 ml/min
$NaBH_4$ concentration	1% (m/v) stabilized with 0.1% (m/v) NaOH
$NaBH_4$ flow rate	3.0 ml/min

4.3 Exposure to Arsenic from Ingested Soil

Ingestion of soil is considered a major non-dietary exposure pathway for many soil contaminants. Arsenic compound would be expected to accumulate and persist in surface soil and assumed approximately 100% of inorganic forms. Numerous studies suggest that people ingest soil from their environment during daily activities, including soil that forms the surface of their yards (Carrizales et al., 2006; Hwang et al., 1997, Garcia-Manyes et al., 2002; Pongratz, 1998).). Generally, the ranges of soil arsenic concentration in undisturbed area were 0.1 to 40 mg/kg (WHO, 2001). Data from Ronphibun showed that arsenic contaminated surface soil ranged from < 10 to 2,123 mg/kg (Williams et al., 1998), 5 to 138 mg/kg (Patarasiriwong and Wongpan, 2004), and 50 to 2,509 mg/kg with mean of 525.33 mg/kg from Suwanmanee (1990) study. While, Visoottiviseth el al. (2002) have been reported that high level of arsenic

concentration in Ronphibun samples soil ranged from 21 to 14,000 mg/kg. The higher silt and clay content in Ronphibun soils leads to higher retention of arsenic (JICA, 2000; Williams et al., 1996).

The recommendation of daily amount of soil ingestion ranged from 50 to 400 mg/d (U.S.EPA, 1997a). In Chapter 3, 35 to 175 mg/d is the suggested range of soil ingestion rates in Thai people. The levels of arsenic in soils were elevated to varying degrees. A number of investigations of residents were conducted to assess potential of soil exposures. Most studies focused on younger children because their typical activities, hand to mouth behaviors, and other behavioral patterns present during childhood could put them at risk for greater exposures than adults (CCME, 1997). Young children play close to the ground and come into contact with contaminated soil especially ages of 1 to 6 years is significantly higher ingestion of soil than the upper 6 years of age (U.S.EPA, 1997a). CCME (1997) reported that 92 to 98% of total inorganic arsenic daily intake resulted form drinking water and food. Approximately 2% was from soil ingestion for all ages. However, young children sustained a greater exposure via soil ingestion about 9% of total daily intake.

In part of chemical exposure from soil, almost policies and studies were very attentive to children because young children are potentially at risk of increased morbidity from arsenic exposure based on differences in pharmacokinetics. In addition, young children may receive higher doses of toxins per unit body weight even if children had the same sensitivity as adults, children could have a greater prevalence of health effects because of their higher daily dose. Thus, exposure from contaminated soil by children is more concerned about ingestion rate and level of concentration than adults. Guideline specifically addressing the care of children exposed to arsenic is currently available. ATSDR established a provisional acute oral minimal risk level (MRL) for arsenic of 0.005 mg/kg/d. The MRL is based on a study of poisoning cases associated with arsenic contamination of soy sauce in Japan, critical effects in the study were facial edema and gastrointestinal symptoms. The MRL includes an uncertainty factor of 10 to account for use of LOAEL rather than NOAEL (ATSDR, 2007).

The health hazard of arsenic contaminated soil depends on both the toxicity of arsenic and the amount of arsenic to which people are exposed through contact with the soil. A major factor determining the magnitude of potential exposures and risks associated with a chemical is its bioavailability. The bioavailability is defined as the fraction of chemical absorbed by the gastrointestinal tract relative to the fraction of chemical absorbed from soil matrix. It allows for adjustment for absorption from a soil in term of absorption factor. It is widely recognized that the bioavailability of chemical in soil tend to be considerably lower than bioavailability from food or water (Ruby et al., 1999).

Studies in animals suggest that bioavailability of arsenic from contaminated soil is less than bioavailability of purified compounds. Tests of soils from arsenic contaminated sites across the country of USA have shown relative bioavailability to be highly site-specific, ranging from less than 10% to near 100% (Robert et al., 2002, 2007; U.S.EPA, 1997b, 2005). Most of U.S.EPA regional was used to availability factor of 10 to 25% for arsenic soil although no human studies of the bioavailability of arsenic from contaminated soil have been published. In recent, information of availability in human is available only for polychlorinated dibenzo-p-dioxins and dibenzofurans, the absorption factor from soil is 0.43 and OEHHS recommended that all others should have an absorption factor of 1 or 100 % (OEHHS, 2003). However, U.S.EPA (1997b) recommended different from OEHHS and adopted a default policy for arsenic bioavailability included the following guidance:

• If site-specific data on arsenic absorption from site wastes are available, they should be relied on in proportion to the confidence placed in the data

• If site-specific data are lacking but mineral speciation data are available indicating 60% or more of the material is in sulfidic form in a fairly insoluble low-arsenic matrix (arsenic can form strong bonds with sulfur), assume a relative bioavailability of 50%.

• If the above data are not available, assume 100% bioavailability or assume a default 80% relative bioavailability for other types of arsenic associated with non-food solid matrices such as soil or waste rock.

Williams et al. (1998) have been investigated the bioavailability of arsenic in soil from Ronphibun *in vitro* by using a physiologically based extraction test. They found that the ranges of bioavailability values were 10 to 35.6% similarity of Ruby et al. (1996) reported that 17 to 50% of bioavailability values from in vitro studies. Risk assessor can be used these bioavailability to calculate risk using an absorption adjusted soil values.

In this Section, inorganic arsenic intakes via ingested soil by people living in Ronphibun area were investigated in both adults and children based on the information of soil ingestion rate in Chapter 3 and arsenic concentration in samples of soil were taken from this site. Then, risk estimates are developed using the deterministic risk characterization approach for hazard quotient and cancer risk with central tendency and reasonable maximum estimates.

4.3.1 Sample Collection and Preparation

For risk assessment, soil means soil and dust particles. Surface soil samples were collected from a depth of approximately 0–15 cm below the surface within a land located in area. Samples were taken from the houses where participants lived and from the places most used by the participants such as agricultural land, school, temple and market. At each site, five soil samples were taken about 500 g which were pooled to one sample per horizon. The soil samples were stored in sealed plastic bags and transported to laboratory. Fifty nine soil samples were obtained for analysis.

After transportation to the laboratory, five hundred gram subsamples of each soil were air-dried until constant weight, homogenized, and ground using a mortar and pestle to pass a 2 mm sieve to remove stones, plant materials, or residues and < 2 mm fraction was retained for analysis. Then, soil samples were packed in individual polyethylene bags until analysis. Subsamples were homogenized again prior to digestion. Inorganic arsenic in soil samples was determined by acid digestion. The 0.5 g of soil sample was accurately weighed, placed in beaker (two replicates for each

sample) and digested with perchloric acid and nitric acid (1:10) solution with 50 ml for 15-18 hrs. Then, the sample was heated by hot plate. Heating was stopped when the dense white fumes of an acid occurred. The digests were cooled, diluted in 50 ml distilled deionized water and filtered the digests through Whatman No. 42 filter paper and collected filtrate in a 100-ml volumetric flask. Make to volume with 5% nitric acid 10 ml and analyze by using HG-AAS.

4.3.2 Determination of Arsenic

Concentrations of arsenic in the samples were measured after acid digestion by using a Perkin Elmer AAnalyst atomic absorption spectrometry interfaced with hydride generation system (HG-AAS).

4.4 Statistical Analysis

In duplicate meal study, descriptive statistics were calculated for characterize the concentration of arsenic in food including min, max, median, mean, SD, and the percentiles. The student's t-test statistics was used for compare arsenic concentration in duplicate meal between genders. In soil ingestion part, arsenic concentration was described with descriptive statistics.

4.5 Reagents and Instruments

Nitric acid (HNO_3), perchloric acid ($HClO_4$) and other chemicals were purchased from Merck. All the reagents were of analytical grade. Standard reference material tomato leaves (SRM-1573a) was obtained from the National Institute for Standards and Technology (NIST), USA. Deionized water was used throughout the

whole experiment for preparation of reagents and standards. Determination of arsenic was performed with a hydride generation- atomic absorption spectrometer (Perkin Elmer AAnalyst). The detection limit of arsenic was 50 µg/g.

4.6 Quality Control

The validity of the analysis was confirmed with the standard reference materials (SRM) tomato leaves (SRM-1573a). The accuracy of the instrumental methods was checked by duplication of the samples, as well as by using a reference material with internal quality control. In each analytical batch at one reagent blank and two spike duplicate samples were included in the acid digests to assess the accuracy of the chemical analysis. Distilled–deionized water was used for all analytical work.

4.7 Interview Application

An interview was conducted to analyze the exposure factors. A structured questionnaire included detailed questions about that variables used to estimate intake namely, body weight, duration frequency, and exposure duration. This form was used to previously study of risk assessment project in Pathumthani province with more than 1,000 people were interviewed (DEP, 2002) with the reliability coefficient value was more than 0.8. Administration of questionnaires was produced by staffs of this research. Two hundred randomly selected people were successfully interviewed in the present study.

4.8 Estimation of Exposure to Arsenic

Inorganic arsenic intake from duplicate meal pathway was estimated by the following equation (U.S.EPA, 1997a):

$$\text{ADDm or LADDm} = \frac{\text{Cm x IRm x ED x EF x AF}}{\text{BW x AT}} \qquad \text{(Eq. 4.1)}$$

where:

ADDm = average daily dose from duplicate meal (mg/kg/d)

LADDm = lifetime average daily dose from duplicate meal (mg/kg/d)

Cm = concentration of arsenic in duplicate meal (mg/g)

IRm = intake rate of duplicate meal (g/d, dry weight)

ED = exposure duration (years)

EF = exposure frequency (day/year)

AF = absorption factor, unitless (AF = 1)

BW = body weight (kg)

AT = averaging time (days), equal to the life expectancy (70 x 365 = 25,550 days) for carcinogen (ATc), and equal to ED x 365 for noncancer estimation (ATnc).

From Eq 4.1, the model was assumed that arsenic contents of duplicate meals were constant for a specific commodity throughout the Ronphibun residents, uniform mixing of arsenic in all samples, and intake rates were constant level for 365 days per year. Only, the deterministic risk assessment or point assessment was estimated in this Chapter. The probabilistic exposure was assessed in the Chapter 6.

Amounts of arsenic intake from soil ingestion both in children and adult were calculated by using the following general equation (U.S.EPA, 1997a):

$$\text{ADDs or LADDs} = \frac{\text{Cs x SIR x AF x ED x EF x CF}}{\text{BW x AT}} \qquad \text{(Eq. 4.2)}$$

where:

ADDs = average daily dose from soil ingestion (mg/kg/d)

LADDs = lifetime average daily dose from soil ingestion (mg/kg/d)

Cs = concentration of arsenic in soil (mg/kg)

AF = absorption factor

SIR = soil ingestion rate (mg/d)

CF = a conversion factor of 10^{-6} (kg/mg)

BW = body weight (kg)

AT = ATc (25,550 days) and ATnc equal to ED x 365 days

In calculation of arsenic intake from soil ingestion, the model was assumed that soil ingested contains a representative concentration of arsenic as modeled by the deposition model and that the concentration was constant over the exposure, arsenic concentration in soil was assumed 100% of inorganic forms, and the uniform mixing of pollutants in the soil. Ingestion of contaminated soil was assumed to take place at a constant level for 365 days per year period and AF used of 0.2 (20% of bioavailability) based on Williams et al. (1998) study. Total of arsenic ingested soil in adults equals rate of ingestion in adults plus children.

4.9 Deterministic Risk Assessment Approach

U.S.EPA policy statement is as follows “a point estimate approach is conducted for every risk assessment; a probabilistic analysis may not always be needed” U.S.EPA (2001a). Deterministic risk assessment (DRA) or point estimate approach uses a single value to represent variables in a risk equation. The output is a point estimate of risk which can be a central tendency estimate (CTE) based on mean or median values, or reasonable maximum estimate (RME) based on the 90^{th} – 99^{th} percentile values for risk, depending on the input values used in the equation. U.S.EPA (1995a) has recommended that using both RME and CTE to convey the variability in risk levels for different individuals in the population.

Estimation of noncarcinogenic effects is evaluated by comparing an exposure level over a specified time period with a reference dose derived for a similar exposure period. This ratio of exposure to reference dose is called a hazard quotient (HQ) and is estimated using the following equation:

$$HQ = \frac{ADD}{RfD} \qquad \text{(Eq.4.3)}$$

where:

HQ = hazard quotient from duplicate meal or soil ingestion pathway (unitless)

ADD = average daily dose from duplicate meal or soil ingestion pathway (mg/kg/d)

RfD = reference dose (mg/kg/d) for ingested inorganic arsenic of 0.0003 mg/kg/d

If the result from ADD divide by RfD exceeds a standard of HQ of 1, there may be concerned for potential noncancer effects.

For cancer effects, risks are estimated as the incremental probability of an individual developing cancer over a lifetime as a result of exposure to the potential carcinogen. Cancer risk was accepted in ranges of 10^{-4} to 10^{-6}. The present study, an acceptable risk of 1×10^{-4} was established for population in Ronphibun area that means only 1 of 10,000 people may be increased cancer effects. Cancer risk characterization can be estimated using the following equation:

$$CR = LADD \times CSF \qquad \text{(Eq.4.4)}$$

where:

CR = cancer risk from duplicate meal or soil ingestion pathway (unitless)

LADD = lifetime average daily dose from duplicate meal or soil ingestion pathway (mg/kg/d)

CSF = cancer slope factor for ingested inorganic arsenic of 1.5 per mg/kg/d

The equation for calculate of cancer risk effect is based on the assumption that dose-response relationship is linear in the low dose portion of the multistage model. Under this assumption the slope factor is constant and risk is directly related to intake. Risks from simultaneous exposure to more than one chemical or from multiple exposure pathways are generally assumed to be additive. These effects can be evaluated by summing the individual estimated HQ or CR and expressed in term of hazard index (HI) and Total Cancer Risk (TCR). HI and TCR can be estimated by the Equation 2.6 and 2.8 in Section 2.6.5, respectively.

CHAPTER V

RESULTS AND DISCUSSION

5.1 Arsenic Intake from Duplicate Meal

5.1.1 Accuracy of the Analysis

The accuracy of duplicate meal analysis was evaluated by analyzing with the standard reference materials (SRM) tomato leaves (SRM-1573a).The average recovery in spiked duplicate meal samples were 95.77% for total arsenic (n=10) and 93.41% for inorganic arsenic (n=10).

5.1.2 Concentrations of Total and Inorganic Arsenic in Duplicate meal

Table 5.1 summaries the total amounts of arsenic, inorganic arsenic and the percentage of inorganic arsenic with respect to total arsenic in duplicate meal samples. The ranges of total arsenic and inorganic arsenic were 0.57 – 1.56 µg/g and 0.16 – 0.42 µg/g, respectively. The percentage of inorganic arsenic in duplicate meal samples ranged 17.74 – 45.16% with a mean of 30.96%. Daily arsenic intake from duplicate meal ranged of 179 – 501 µg/d for total arsenic with mean of 318 µg/d and 56.6 – 146 µg/d for inorganic arsenic with mean of 97 µg/d (Table 5.2).

Table 5.1 Concentration of total arsenic and the percentage of inorganic arsenic

Statistical value	Total arsenic (µg/g)	Inorganic arsenic (µg/g)	Percent of inorganic arsenic
Min	0.57	0.16	17.74
Mean	0.98	0.30	30.96
SD	0.23	0.06	4.85
5^{th} percentile	0.63	0.19	23.37
25^{th} percentile	0.81	0.25	27.67
Median	0.95	0.29	30.85
75^{th} percentile	1.14	0.35	34.21
90^{th} percentile	1.30	0.38	36.44
95^{th} percentile	1.36	0.40	39.24
Max	1.56	0.42	45.16

Table 5.2 Daily intake of arsenic from duplicate meal

Statistical value	Total arsenic (µg/d)	Inorganic arsenic (µg/d)
Min	175	56.5
Mean	318	97
SD	76.7	22.2
5^{th} percentile	203	62.3
25^{th} percentile	254	80
Median	312	95.5
75^{th} percentile	380	113
90^{th} percentile	424	128
95^{th} percentile	442	133
Max	501	146

Amount of food consumption, body weigh, and concentration of inorganic arsenic in samples were different between genders and individuals. However, there was no significantly different according to inorganic arsenic intake rate per kg per day when testing by Student's t-test statistics (p-value = 0.82). Table 5.3 summarizes the rate of inorganic arsenic intake per kg per day.

Table 5.3 Inorganic arsenic intake by gender

Statistics value	Inorganic arsenic concentration (µg/kg/d)	
	Female	Male
Min	1.09	1.02
Mean	1.62	1.68
SD	0.30	0.29
5^{th} percentile	1.14	1.21
25^{th} percentile	1.38	1.41
Median	1.64	1.69
75^{th} percentile	1.85	1.93
90^{th} percentile	2.03	2.04
95^{th} percentile	2.09	2.06
Max	2.10	2.09

5.1.3 Description of Exposure Factors

The principal exposure factors that have been taken into account to carry out the risk assessment calculations are showed in Table 5.4 and Table 5.5. LADD estimation were used the same parameters of ADD except averaging time (AT is fixed to 25,550 days both CTE and RME estimates). Exposure parameters were evaluated

from interviewed data. The life expectancy for Thai people ranged 68.15 - 73.58 years (the census data from 2005 – 2015). The value of 70 years was selected for this study.

Table 5.4 Distribution of exposure parameters

Statistical value	Exposure parameters				
	Body weight (kg)	Exposure duration (years)	Exposure frequency (days/year)	Averaging time (days)	Intake rate (g/d)
Min	30	2	200	730	273
Mean	58.3	27.5	350	10,220	336
SD	10	17	3,062	6,252	39.2
5^{th} percentile	45	5	285	1,825	283
25^{th} percentile	51	15	353	5,475	299
Median	57.5	24	365	8,760	311
75^{th} percentile	65	36	365	13,323	343
90^{th} percentile	70.2	55	365	20,075	385.6
95^{th} percentile	75	63	365	22,995	405
99^{th} percentile	80	68	365	25,185	438
Max	90	71	365	25,915	469

Table 5.5 Exposure parameters for ADD or LADD estimation

Parameter	Symbol	Units	Parameter characteristic	
			CTE	RME
Exposure duration	ED	years	28 (mean)	63 (95^{th} percentile)
Exposure frequency	EF	days/year	350 (mean)	365 (90^{th} percentile)
Averaging time				
- Carcinogen	ATc*	days	25,550	25,550
- Noncarcinogen	ATnc	days	10,220 (mean)	22,995 (95^{th} percentile)
Body weight	BW**	kg	60 (mean)	60 (mean)
Concentration of arsenic in meal	Cm	mg/g	0.0003 (mean)	0.0004 (95^{th} percentile)
Intake rate of meal	IRm	g/d	336 (mean)	405 (95^{th} percentile)

*For carcinogen effect, ATn is fixed equal to 70 year x 365 day = 25,550 days; for noncancer effects, ATnc = ED x 365.

**U.S.EPA recommended that should be selected mean of body weight in calculation risk because it has reason to toxicology evaluation. Mean of body weight from data was 58.26, approximately 60 kg (U.S.EPA, 1997a).

5.1.4 Point Estimate of Exposure Assessment

In the present study, the conceptual model was based on the exposures of the Ronphibun residents. The exposure scenario in this situation was narrowed down to the intake of inorganic arsenic through duplicate meal samples. The exposure assessment of ingested inorganic arsenic can be estimated by Equation 4.1 using the values of CTE and RME in Table 5.5. Table 5.6 summarizes the outcomes of the ADD and LADD estimated for inorganic arsenic with the duplicate meal pathway. The ranges of inorganic arsenic intake were 0.0016 and 0.0027 mg/kg/d for ADD by using CTE and RME estimate, respectively; 0.0006 and 0.0024 mg/kg/d for LADD by using CTE and RME estimate, respectively.

Table 5.6 ADD and LADD from duplicate meal

Pathway	ADD (mg/kg/d)		LADD (mg/kg/d)	
	CTE	RME	CTE	RME
Duplicate meal	0.0016	0.0027	0.0006	0.0024

5.1.5 Deterministic Risk Characterization of Arsenic

Risk from ingested inorganic arsenic in duplicate meal can be calculated by using Equation 4.3 and 4.4 for HQ and CR, respectively. The results of the deterministic risk estimates, HQ for CTE and RME estimates from arsenic exposure via duplicate meals were of 5.33 and 9.00, respectively. In this case the HQ for arsenic is higher than 1. This indicates that noncancer health effects from arsenic are likely. The ranges of cancer risk were of 9.00×10^{-4} to 3.6×10^{-3} based on RME and CTE estimates, respectively. In term of 3.6×10^{-3} means about 3 to 4 of 1,000 people may be increased cancer effect from the background. The cancer risk from duplicate

meal intake was excess acceptable level of 1 x 10^{-4}. The summaries of these results are shown in Table 5.7.

Table 5.7 Risk characterization of arsenic from duplicate meal pathway

Pathway	HQ		CR	
	CTE	RME	CTE	RME
Duplicate meal	5.33	9.00	9.00 x 10^{-4}	3.6 x 10^{-3}

5.2 Discussion of Arsenic Intake

The major difference between the present study and previous studies in Ronphibun area is the use of inorganic arsenic contents in duplicate meal rather than total arsenic to estimate exposure. Levels of total arsenic in duplicate meal samples ranged of 175 to 501 µg/d. While, a ranges level of inorganic arsenic (the form of most concern) were 56.5 to 146 µg/d. Dietary intake of inorganic arsenic was less than 3 times of total arsenic. The average percentage of inorganic arsenic with respected to total arsenic was 30.96% (17.74 to 45.16%). It is also important to recognize that the fraction of inorganic arsenic in food items varies widely (Schoof et al., 1999). Meacher et al. (2002) suggested that inorganic arsenic in food composes about 20% of the total arsenic. Mohri et al. (1990) reported that the diet in Japan was contained 5.7 to 17% of inorganic arsenic forms while Kile et al. (2007) estimated that the average inorganic arsenic concentration comprised 82% of the total arsenic detected in the dietary samples and this is similar to values reported by Smith et al. (2006) who reported that inorganic arsenic made up 87% of the total arsenic measured in rice and 96% of the total arsenic measured in vegetables commonly consumed in Bangladesh. Our estimated inorganic fraction is slightly lower, may be came from the inorganic fraction in homogenized duplicate dietary samples rather than individual food items and the different of food types. However, the study on bioavailability of

arsenic in cooked rice or other foods is limited, the only data generated by Juhasz et al. (2006) stated that 90% of the arsenic is bioavailability for rice varieties with high inorganic arsenic content.

Food and beverages are the most important sources of exposure to arsenic for general population. Dietary total arsenic intakes estimated from various countries ranged between lower than 10 µg/d and 200 µg/d (WHO, 2001). Generally, the amount of total arsenic intake was about 50 µg each day and the inorganic arsenic was of 3.5 µg/d. Dietary intakes of inorganic arsenic in U.S. people have been estimated to be 1 to 20 µg/d with grains and produce expected to be significant contributors to dietary inorganic arsenic intake (Gunderson, 1995; Tao and Bolger, 1999; U.S.FDA, 1997). Recent estimates of the mean daily intake of total arsenic in food for adults are as follows: 42 µg (ranged 22.5 - 78.7 µg) in Canada, 56 µg (ranged 27.5 - 92.1 µg) in the United States, 120 µg in the United Kingdom, 150 µg in New Zealand, 286 µg in Spain, 210 µg in Japan, and 180 µg in Bangladesh. Seafood was the major source of arsenic, contributing 56 - 96% of the total (ANZFA, 1994; Dabeka et al., 1993; Huang et al., 2003; Ohno et al., 2007; Tao and Bolger, 1998; Tsuda et al., 1995; UKMAFF, 1999; Urieta et al., 1996; Yost et al., 1998). However, in arsenic affected areas it was found that the amount of arsenic intake higher level such as in Bangladesh, the ranges of arsenic intake from duplicate meal were 43 - 490 µg/d (Ohno, et al., 2007). The average daily total arsenic intake calculated in Kile et al. (2007) study was 174 µg/d, which is considerably lower than the 515 µg/d estimated in an earlier study for an adult Bangladeshi (Watanabe et al., 2004). The present study in arsenic affected area of Ronphibun, The average intake of total arsenic was 318 µg/d and 97 µg/d of inorganic arsenic intake via duplicate meal method.

Table 5.8 shows the comparison of the present study results with PTDI, acute MRL, and Thai FDA recommendations. All of duplicate meal samples were below the standards. Thai FDA has established a permissible exposure limit of 2 mg/kg/d for total arsenic in foods (Thai FDA, 2003). By assuming 30.96% of arsenic intake was in inorganic form, it follow that the average daily intake was about 0.62 mg/kg/d of inorganic arsenic. The results of ADD and LADD from the present study were 0.0006

to 0.0027 mg/kg/d, lower than this standard. Concentrations of arsenic were reported in the present study lower than those previously reported by Thailand agency or Thai researchers (Chantarawijit et al., 2000; DMS, 2000; Tongboriboon, 1997; Vitayavirasuk, 1999). The principal reason, because the participants and the most people in Ronphibun have been avoided eating contaminant high level of arsenic in well or ground water. Before 2000, the drinking water samples (well or groundwater) from Ronphibun area have exceeded by 100 times of drinking water standard of Thailand, 0.05 mg/l. After that many people try to avoid drinking arsenic contaminated water. They obtain drinking water from other sources such as rainwater or bottle water. The report has been showed that 77% and 13% used to rainwater and piped water for drinking, respectively. Wongsanoon et al. (2000) reported that the ranges of rainwater in this area were 0.26 – 1.29 µg/l, below Thai standard and WHO regulation level.

Table 5.8 Regulations of arsenic in food and water

Agencies	Description*	Information
Thai FDA	Food	2 mg/kg/d (total arsenic)
WHO	PTWI	0.015 mg/kg/wk (inorganic arsenic)
	PTDI	0.0021mg/kg/d
	Drinking water	0.01 mg/l (inorganic arsenic)
USDA	Drinking water	0.01 mg/l (inorganic arsenic)
ATSDR	acuteMRL	0.005 mg/kg/d (inorganic arsenic)

*PTWI = provisional tolerable weekly intake; PTDI = provisional tolerable daily intake; acuteMRL = a provisional acute MRL for oral exposure to arsenic. Source: ATSDR (2007)

Table 5.9 summarizes several attempts to estimate the arsenic intake from food and drinking water both in arsenic contaminated areas (all counties except USA and Canada) and non contaminated areas. Compared to the residents of non

contaminated areas, people living in the arsenic contaminated areas could consume higher than approximately 30 times the amount of arsenic.

Table 5.9 Estimation of total arsenic intake in Asia and other area populations*

Population	Arsenic from diet (µg/d)	Arsenic from water intake (µg/d)	Total arsenic intake (µg/d)	Methods	Reference
India	285	800-1000	1085-1285	Assuming 200 µg/l WI 3 l/d	Chowdhury et al. (2001)
Bangladesh	120-214	395-460	515-674	Assuming 100 µg/l WI 3 l/d	Watanbe et al. (2004)
Taiwan	62-292 (iAs)	NA	NA	Yam and rice samples analyzed	Schoof et al. (1999)
USA and Canada	8.3-14 (iAs) 4.8-12.7 (iAs)	NA	NA	iAs accounted for 21-40% of total As	Yost et al. (1998)
Thailand	57-146 (iAs)	-	-	Duplicate meal including drinking water survey and analysis	Present study

* iAs = inorganic arsenic; NA = no available data; WI = water intake

U.S.FDA determined the mean total arsenic daily intake from food in 1986 to 1994 to be 33 µg. Seafood contributed 88% of the average daily total intake. Appling 12% estimate of inorganic arsenic intake would yield 4 µg/d (Gunderson, 1995; Schoof et al., 1999; U.S.FDA, 1997). Similarity, the reported of U.K.FSA (UK of Food standards Agency) that estimated the mean daily total arsenic intake approximately 65 µg/d. By assuming only 8% of arsenic intake was in the inorganic form, it follow that the average daily intake was about 5 µg of inorganic arsenic (DEFRA, 2002; FSA, 2004). While, the report of Kile et al. (2007) that determine the daily arsenic intake in Bangladesh about 174 µg/d and applying 82% estimate of inorganic arsenic intake was 142.68 µg/d. The present study, the average total arsenic was of 318 µg/d which higher than Kile et al. (2007) data but the level of inorganic arsenic was found lower of 97 µg/d. These results were difference may be from types of food, pattern of consumption and cooking methods. U.S.EPA estimates that preparing foods with arsenic containing water may increase arsenic content by as much as 10 to 30% for most foods, beans and grains that absorb water when cooked may absorb up to 200 to 250% (Mead, 2005). After cooking, most of water is evaporated but arsenic contained in the initial water stays with the food and is concentrated. Aside from the arsenic exposure through water consumption, food can be a significant source of arsenic not only because some foodstuffs are prepared with arsenic contaminated water as a source for indirect water intake but also because they contain a significant amount of arsenic. The duplicate meal method for estimation of the daily arsenic intake can take into account the effects of the cooking process or cooking water. Duplicate diet studies are considered to be more accurate at estimating personal exposures because they account for the individual food and water source, the type and quantity of food items consumed, cooking method, and the agricultural conditions under which the food is cultivated (WHO, 1985). It is important to note that the estimates derived from duplicate diet studies depend on the dietary habits of the participants in local area and may not be generalized to other regions and in this study the impact of seasonal variation, the level of physical activity, or other factors on the intake rate in the population have not been adequately evaluated.

Point estimate of risk characterization uses a single value to represent variable in an equation. CTE is considered to be a measure of mean or median while, RME is represented the highest exposure to occurs (the 90^{th} – 99^{th} percentiles). The difference between the CTE and RME gives an initial impression of the degree of variability in exposure between individual in an exposure population. The present study, the RME of HQ and CR were higher than 2.5 - 6 times of CTE estimate of ingested inorganic arsenic in duplicate meal pathway.

The result of deterministic risk assessment in term of HQ from exposure arsenic via duplicate food was greater than 1 (HQ = 5.33-9.00) indicated that risk is probably to result in any adverse health effect. While, the ranges of CR level were 9.0 x 10^{-4} to 3.6 x10^{-3} that increased than safety risk was set of 1 x 10^{-4}. However, the present results were similar to previous studies. DMS (2003) reported that the increased cancer risk from consumption of food and water in this site was 2.9 x 10^{-2} based on exposure duration of 20 years. Vitayavirasuk (1999) presented that 1.9 x 10^{-5} to 4.3 x 10^{-4} of cancer risk in Ronphibun residents from drinking water. In addition, Chantarawijit et al. (2000) have been reported that the ranges of cancer risk from exposed to arsenic in drinking water were 5 x 10^{-4} to 4 x 10^{-2} and 8 x 10^{-4} to 4 x 10^{-3} from ingested arsenic from food. In the world, cancer risk and HQ from exposed to arsenic from food and water have been reported that less than 10^{-6} to over 10^{-4} depending on levels of concentration and exposure factors (ATSDR, 2007). The uses of RME calculate that based on high end values for dealing variability or uncertainty in risk characterization step, may be resulted of high risk values thus before in conclusion should be investigated these effects. U.S.EPA (2001a) suggested that risk estimators should be estimated risk by using probabilistic risk assessment for separate an uncertainty effects. U.S.EPA (1989) recommended that should inclusion of both CTE and RME in the risk assessment process. Its results may benefit from understanding the reasons for the differences and the relating strengths of the different approaches. HQ and CR results from using the deterministic approach for a CTE and RME in this Section are compared with risk estimates at the 50^{th} percentile and 95^{th} percentile obtained from Monte Carlo analysis in next Chapter.

5.3 Exposure to Arsenic from Ingested Soil

5.3.1 Accuracy of the Analysis

The accuracy of analysis was evaluated by analyzing the standard reference materials (SRM) tomato leaves (SRM-1573a).The average recovery of arsenic in standard reference material was 95% (n=10) and the mean recovery in spiked soil sample was 92% (n=10).

5.3.2 Arsenic Concentration in Soil

Concentration of arsenic in surface soil samples varied between 26 to 867 mg/kg with mean of 222.05 mg/kg, median of 151 mg/kg, and the 95th percentile of 793 mg/kg. The distributions of arsenic concentration are presented in Table 5.10.

Table 5.10 Concentration of arsenic in soil samples (dry weight)

Statistical value	Arsenic (mg/kg)
Min	26
Mean	222
SD	203
5th percentile	27
25th percentile	74
Median	151
75th percentile	313
90th percentile	466
95th percentile	793
Max	867

5.3.3 Description of Exposure Factors

For adults, the exposure parameters are presented in Table 5.11. Exposure duration in this case resulted from total duration for exposure in adults is subtracted by exposure duration in children. Arsenic concentration in soil was selected from median value because this value covered about 50% both the lower and higher concentration levels than the truly average value and the 90^{th} percentile for the upper value that it extended about 93% of arsenic concentration in all soil samples. Soil ingestion rates were derived from the study in Chapter 3; 35 mg/d for central tendency estimate (CTE) and 120 mg/d for reasonable maximum estimate (RME) in adults; 50 mg/d and 175 mg/d for CTE and RME estimates in children, respectively.

For children, body weight was derived from the report of the Department of Environmental Promotion, Thailand (DEP, 2005) because this study can not interviewed children. The average of body weight was of 15.42 kg with ranged 7 to 32 kg based on 1 to 6 years (n = 115). Exposure duration of 2 years for CTE estimate and 6 years for RME estimate are referenced from Exposure Factors Handbook of U.S.EPA (1997a). Absorption factor, exposure frequency, and arsenic concentration in soil used to the same values with adults both CTE and RME estimates. Soil ingestion rate was derived from Chapter 3. Table 5.12 shows exposure parameters for children.

Table 5.11 Description of exposure parameters for adults

Parameter	Symbol	Units	Parameter characteristic	
			CTE	RME
Exposure duration	EDa	years	26 (mean)	57 (95^{th} percentile)
Exposure frequency	EFa	days/year	350 (mean)	365 (90^{th} percentile)
Averaging time				
- Carcinogen	ATca	days	25,550	25,550
- Noncarcinogen	ATnca	days	9,490	20,805
Body weight	BWa	kg	60 (mean)	60 (mean)
Absorption factor	AF	-	0.2	0.2
Soil Ingestion rate	SIRa	mg/day	35 (mean)	120 (95^{th} percentile)
Arsenic concentration in soil	Cs	mg/kg	151 (median)	466 (90^{th} percentile)

Table 5.12 Description of exposure parameters for children

Parameter	Symbol	Units	Parameter characteristic	
			CTE	RME
Exposure duration	EDc	years	2	6
Exposure frequency	EFc	days/year	350	365
Averaging time				
- Carcinogen	ATcc	days	25,550	25,550
- Noncarcinogen	ATncc	days	730	2,190
Body weight	BWc	kg	15 (mean)	15 (mean)
Absorption factor	AF	-	0.2	0.2
Soil Ingestion rate	SIRc	mg/day	50 (mean)	175 (95^{th} percentile)
Arsenic concentration in soil	Cs	mg/kg	151 (median)	466 (90^{th} percentile)

5.3.4 Point Estimate of Exposure Assessment

5.3.4.1 Soil exposure assessment for children

The exposure assessment of soil ingested arsenic can be estimated by the Equation 4.2 with parameters in Table 5.12. The results of ADD and LADD estimates are presented in Table 5.13. The ranges of arsenic intake by soil in children were of 0.00109 to 0.0000965 mg/kg/d (CTE to RME of ADD estimation) and 0.000093 to 0.00000276 mg/kg/d (CTE to RME of LADD estimation).

Table 5.13 ADD and LADD from soil exposure assessment

Group	ADD (mg/kg/d)		LADD (mg/kg/d)	
	CTE	RME	CTE	RME
Children	9.65×10^{-5}	1.09×10^{-3}	2.76×10^{-6}	9.3×10^{-5}
Adults	1.68×10^{-5}	1.86×10^{-4}	6.27×10^{-6}	1.52×10^{-4}

5.3.4.2 Exposure assessment for adults

Arsenic intake by soil in adults ranged from 0.000152 to 0.00000627 mg/kg/d based on LADD estimation and 0.000186 to 0.0000168 mg/kg/d based on ADD estimation. Comparison ADD and LADD of arsenic from soil exposure between adult and children are presented in Table 5.13. Next, the LADD is multiplied by the oral cancer slope factor for arsenic, 1.5 per mg/kg/d, to determine cancer risk (CR). The ADD is divided by reference dose for arsenic of 0.0003 mg/kg/d, to determine the HQ.

5.3.5 Deterministic Risk Characterization of Arsenic

5.3.5.1 Characterization of risk from ingested soil

The results of risk estimates, HQ form CTE and RME estimates in children were of 0.32 and 3.62, respectively. HQ of ≤ 1 means that the estimated dose is equal or below the safe dose and noncancer health effects are unlikely. HQ greater than 1 indicates that the estimated dose exceeds the safe dose and noncancer health effects cannot be ruled out. In adults, risk calculation included exposure results of children and results of exposure in adults via soil ingestion for estimate HQ and CR. HQ form CTE and RME estimate were of 0.38 and 4.24, respectively. While, the

ranges of cancer risk in children were of 4.14×10^{-6} to 1.4×10^{-4} based on CTE and RME estimates, respectively. In term of 1.4×10^{-4} from RME cancer risk estimate means 1 of 10,000 of children may be increased cancer effect from the background of cancer prevalence. In adults, cancer risk estimates by CTE and RME were 1.25×10^{-5} and 3.7×10^{-4}, respectively. The summaries of HQ and CR are presented in Table 5.14.

Table 5.14 HQ and CR of arsenic from soil ingestion

Group	HQ		CR	
	CTE	RME	CTE	RME
Children	0.32	3.62	4.14×10^{-6}	1.4×10^{-4}
Adults	0.38	4.24	1.25×10^{-5}	3.7×10^{-4}

5.3.5.2 Total risk characterization of arsenic in adults

Hazard index (HI) of arsenic from duplicate meal and soil ingestion pathways in adults were 5.71 and 13.24 based on CTE and RME, respectively. Total cancer risk from exposure to contaminated arsenic in all exposure pathways were 9.13×10^{-4} and 3.97×10^{-3} based on CTE and RME, respectively. The results of total deterministic risk characterization of arsenic in adults are presented in Table 5.15 Table 5.16 summarizes the risk contribute from duplicate meal and soil ingestion pathway.

Table 5.15 Total risk in adults from exposure to arsenic in all exposure pathways

Route	HQ		CR	
	CTE	RME	CTE	RME
Duplicate meal	5.33	9.00	9.0×10^{-4}	3.6×10^{-3}
Soil	0.38	4.24	1.25×10^{-5}	3.7×10^{-4}
Total	5.71	13.24	9.13×10^{-4}	3.97×10^{-3}

Table 5.16 Percentage of risk contribute

Pathway	Contribution of Risk (%)				
	CTE of HQ	RME of HQ	CTE of CR	RME of CR	Average
Duplicate meal	93.35	68	98.58	90.68	88
Soil ingestion	6.65	32	1.42	9.32	12

5.4 Discussion for Part of Risk from Soil intake in Children and Total Risk in Adults

Arsenic concentrations in all surface soil samples (Table 5.10) were significantly greater than the Acts of Soil Standard in Thailand as 3.9 mg/kg of arsenic in soil for residential and agricultural land and 27 mg/kg for others land (ONEP, 2004). The minimal concentration from soil sample in the present study was 26 mg/kg which was about 7 times higher than the soil standard value for residential and agricultural land and more than 222 times when comparison with the maximum of arsenic concentration in soil sample (867 mg/kg). The higher arsenic concentrations were results of both higher anthropogenic disturbance and natural soil factors. Many studies reported that had significantly higher background arsenic

concentrations in soils from Ronphibun. However, the evaluation of arsenic in soil was started at about 20 years, ago. Thus, it may be was no really background concentration of arsenic in soil. Since arsenic is expected to remain in soil for centuries or longer.

The results of arsenic soil concentrations in this study were considerably lower than that obtained by Visoottiviseth el al. (2002) (ranged 54-1,860 mg/kg) and similar to the previous studies of DMS (2000) (ranged 1.11-5,300 mg/kg), Patarasiriwong and Wongpan (2004) (ranged 9.6-1,549 mg/kg), Suwanmanee (1990) (ranged 50-2,509 mg/kg), Tongboriboon (1997) (ranged 100-1,845 mg/kg), and Williams et al. (1998) (ranged < 10-2,123 mg/kg). These results can be explained that the original problem of high arsenic accumulation in Ronphibun's soil have not completely managed to solve the problem. JICA (2000) have been reported that should be treated of contaminated soil more than hundred thousand cubic meter in Ronphibun area. The budget for cleanup contaminated soil will be spent over 600 million baht. Hence, the arsenic problem remained still for long periods in this site. Consequently, future generations of residents may also be at risk since arsenic remains in soil for hundreds to thousands of years.

The average contribution of risks in adults from soil ingestion were 85% and 35% of HQ and CR values, respectively that resulted from in children exposure. Generally, children ingest soil more soil than adults because the hand to mouth activity and behaviors patterns. Almost policies and studies of chemical exposure from soil are very attentive to children because children may receive higher doses of toxins per unit body weight even if they had the same sensitivity as adults, children could have a greater prevalence of health effects because of their higher daily dose. Thus, exposure from contaminated soil by children is more concerned about ingestion rate and level of concentration than adults. The HQ of 3.62 in children indicated that exposed to arsenic by soil in children have greater noncancer effects. The comparison the exposed to arsenic in children (0.000096 – 0.001 mg/kg/d) with acute minimal risk level of 0.005 mg/kg/d (ATSDR, 2007) found that a child living in Ronphibun was exposed of arsenic lower than minimal risk level of 5 – 52 times. The minimal of

only 5 times should be concerned. Concern for acute toxicity of arsenic contaminated soil is related to the occasional ingestion of large amounts of soil. When surface soil in a residential area is contaminated, it is expected that chronic exposures to the contaminants will occur and that cleanup of this soil will be based on an evaluation of long term exposure (ATSDR, 2007). Thus, in this site risk manager should be focused on long time exposure than short period for planning on solving a risk.

Rakwong (1999) reported that the average arsenic concentration of surface soil was 93.34 mg/kg with ranged 7.51 to 510.93 mg/kg and the ranges of total cancer risk were of 8.11×10^{-5} to 6.29×10^{-5}. Chantarawijit et al. (2000) have been estimated that cancer risk from soil ingestion of 2×10^{-4}. The result from DMS (2003) indicated the excess cancer risk of adults in Ronphibun from ingested soil was 2.56×10^{-5}. ATSDR (2007) have been reported that arsenic ingestion for people exposed to Anaconda residential soil ranged of 0.00005 to 0.00053 mg/kg/d with arsenic concentration of 250 mg/kg. To estimate cancer risk, the resulting estimated excess cancer risk to 9.4×10^{-5}. The reports from Thai agencies or researcher have been estimated cancer risk values different from the present study that resulted of their are estimated by using the difference of arsenic concentration in soil, exposure duration, U.S.EPA's exposure references such as exposure duration of 30 years, soil ingestion rate of 100 mg/d for children and 50 mg/d for adults. However, most of studies were the ranges of 10^{-4} to 10^{-5} similarity the results of the present study.

The results from Section 5.3.5.2, total risk in adults, percent of risk has contributed from duplicate meal pathway higher than from soil ingestion pathway. However, arsenic in food and water were transferred from contaminated arsenic soil. The average contribution of soil ingestion to risk of arsenic in the present study was about 12% and more than approximately 88% of risk values resulted from duplicate meal exposure that similar the foreign studies, normally about of 10% from soil ingestion pathway and approximately 90% from food and water consumption (ATSDR, 2007; Carrizales, et al., 2006; Simon, 1998). Cancer risk estimates by RME values from soil ingestion pathway were 1.4×10^{-4} in children, 3.7×10^{-4} in adults, and total cancer risk from soil ingestion and duplicate meal pathway in adults ranged

9.13×10^{-4} to 3.97×10^{-3}. These were higher than the acceptable excess cancer risk was set in the present study as 1×10^{-4}. It means that more than one person in ten thousand to thousand people probably will develop cancer by exposure to the medias investigated. Cancer risk was increased than acceptable risk may be that resulted from variability or uncertainty of exposure parameters can affected of risk value, especially in children. In this case, U.S.EPA recommended that should be estimated risk by using probabilistic risk assessment for separate an uncertainty effects. In next Chapter, characterization of risk was estimated by using Monte Carlo method for comparison risk values between deterministic and probabilistic risk assessment.

CHAPTER VI

PROBABILISTIC RISK CHARACTERIZATION OF ARSENIC

6.1 INTRODUCTION

The concept of risk comes form the recognition of uncertainty. Risk implies that a given action has more than one set of outcomes each being equally or not equally likely to occur. U.S.EPA separated risk characterization to two methods: deterministic risk assessment (DRA) and probabilistic risk assessment (PRA). DRA uses a single value to represent variables in a risk equation. The output of point estimate risk assessment is a point estimate of risk while PRA uses probability distribution for variables in risk equation. The output of PRA is a probability of risk that reflects the combination of the input probability distribution. Since, the result of DRA does not lend itself to characterize of risk such as quantitative uncertainty data. PRA can provide unique and important supplemental information that can be used in making decision. PRA is a general term of risk assessment that use probability models to represent the likelihood of different risk levels in a population or to characterize uncertainty in risk estimates (U.S.EPA, 1995, 2000b).

The basic idea of PRA is quite simple. The purpose of risk managers is to provide protection for the general public or specific subpopulation. Each individual in a specific human population is subject to a personal concentration exposed for a given compound. The values of chemical concentration exposure are varies among individuals. In addition, individuals vary in other exposure factors. All of the variation can be quantified by probability distributions. Probabilistic approaches of risk

assessment are receiving increasing attention, both regarding exposure assessment and risk characterization (Baird et al., 1996; Jager et al., 2001; Slob and Pieters, 1998).

Probabilistic analyses have been recognized in regulatory guidance and U.S.EPA has published a document of principles for conducting Monte Carlo analyses (MCA) in 1997 (U.S.EPA, 1997d). MCA is perhaps the most widely used probabilistic method in PRA. MCA is a specific probabilistic method that uses computer simulation to combine multiple probability distributions in a risk equation. MCA has been used in modeling since 1946 when Stanislaw Ulam used MCA to conduct uncertainty analysis at Los Alamos during the conceptual stage of the hydrogen bomb project. The application of PRA to human health risk assessment is a relatively recent development that was facilitated by development of statistical sampling techniques to obtain a probabilistic approximation to the solution of a mathematical equation and increased speed and capacity of modern computers which can support the intensive computational requirements of MCA. Computer and commercial software are currently available which enable risk assessors to make PRA calculations in minutes, that only a few years ago would have required days (Jager et al., 2001; Mckone, 1994; Williams and Paustenbach, 2000).

MC method is contrasted to the deterministic method used to generate specific single number or point estimates of risk. For example, children exposure to chemical carcinogenic soil contaminant via ingestion will illustrate the difference. The intake rate of contaminant is the product of its soil concentration and the amount of soil consumed within a time frame. It is evident that both parameters will vary of soil concentrations of the contaminant at various locations at the site and children in how much contaminated dirt they ingest in a given period. Further, the actual distribution of values for each of these factors may be uncertain. MC simulation would involve many calculations of the intake rate rather than a single calculation; for each calculation, the computation would use a value for each input parameter randomly selected from the probability density function for that variable. Over multiple calculations, the simulation uses a range of values for the input parameters that reflects the probability density function of each input parameters. Thus, the repetitive

calculations take many randomly selected combinations of the amount of soil consumed and soil contamination levels into account, generating a probability density function or cumulative density function for the output. Based on the distribution of the output, a risk level representing the high end or desired level of probability can be identified. This simple example suggest a MC simulation in which variability and uncertainty are not treated separately, the probability density function for each input parameter would reflect both the inherent parameter heterogeneity and uncertainty about the accuracy of measurements. Thus, the output probability distribution similarly would reflect both undifferentiated variability and uncertainty. However, it may be important for some purposes to disaggregate the effects of variability and uncertainty on the output which can be achieved through second order MC simulation or other methods (Binkowitz and Wartenberg, 2001; Finley and Paustenbach, 1994; Vose, 2000). If uncertainty in only a few parameter value is of interest first order MC simulation can yield the same results as a second order MC simulation but without the time and effort of second order MCA. U.S.EPA suggested that when only few sources of parameter uncertainty are quantified first order MC simulation is preferred over second order MC simulation because the approach is easier to use and communicate (U.S.EPA, 2001a). Identifying key sources of variability can help target risk reduction measures, while identifying key sources of uncertainty can help target addition studies if the assessment needs to be refined (Oberg and Bergback, 2005; Hamed, 2000; Sheppard, 1995).

In the present study, a few uncertainty parameters of concentration term and absorption factor for soil ingestion studies were classified both in children and adults parts, and duplicate meal part is separated of concentration value only for uncertain factor. The following variables were considered variable: soil ingestion rate, exposure duration, exposure frequency, averaging time, and body weight. In addition, the object of this study is estimated risk in specific area and specific subpopulation, may be it slightly difference between inter-individuals or other exposure factors. Thus, the first order MCA uses for estimate risk from exposure to arsenic via soil and duplicate meal pathways.

The aims of this Chapter were to estimate risk by using probabilistic risk assessment approach and compared the results of risk from using deterministic risk assessment, before an answered the question, “What is the probability that risks to an exposed people will exceed 1.0×10^{-4} for cancer effects or 1 for noncancer effects?”

6.2 Risk Characterization of Arsenic from Soil Intake in Children

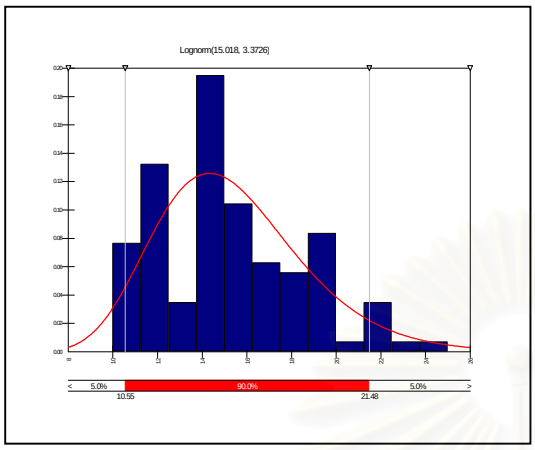
6.2.1 Risk characterization model

The structure of a probabilistic model is similar to that of a deterministic model with all the operators that link the variables together except that each variable is represented by a distribution function instead of a single value. Thus, it allows taking the variability of input data into account which provides far more realistic results than that produced by simple deterministic approach. The risk characterization models were referenced from U.S.EPA. Noncancer risk was estimated by model following: HQ = ADD / RfD (Eq 4.3), where ADD and RfD represent the average daily dose and reference dose, respectively. The estimated cancer risk was calculated according to the formula CR = LADD x CSF (Eq 4.4), where LADD and CSF represent, respectively, the lifetime average daily dose and cancer slope factor.

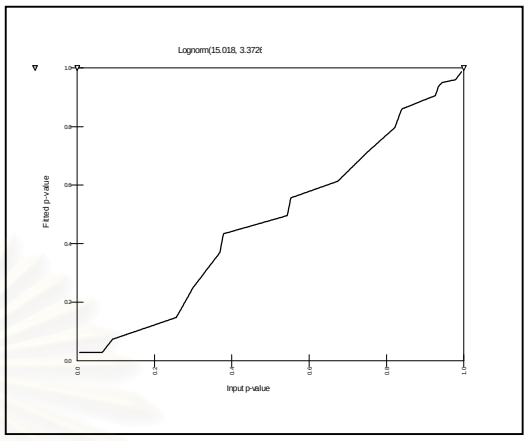
6.2.2 Parameter probability distributions for input variables

The distributions for all variables were interpolated with the software @RISK (Version 4.5.5, Palisade Corp., USA) in combination with Microsoft Excel for this analysis by following procedure: graphic choice of the shape of the distribution and verification that it was not rejected by the Anderson-Darling test which was appropriate for considering the values of the distribution tail. Statistically the goodness of fit distribution was determined by fitting difference probability

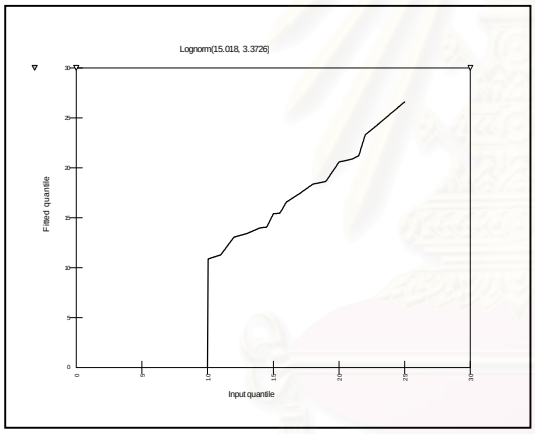
distributions to the data set and finally ranking them by test value. Inspection of P-P graphs and Q-Q graphs was carried out to determine if there was any systematic variation in the magnitude or residuals. For the best fitted distribution the distribution parameters were estimated by maximum likelihood estimators. The inputs bearing the most uncertainty are evaluated by applying probability distributions available in @RISK, a total thirty two distributions are currently available in @RISK. After probability distributions were defined for each of random variables analyzed in this study, the risk model was analyzed with Monte Carlo simulation. The model was simulated for about ten thousand iterations or it can set to iterate as a specified stopping rule is satisfied and results on the probabilities for the range of all possible outcomes were obtained (Palisade, 2005). It is natural in a risk analysis model for its variables to be negatively or positively correlated with each other. However, this study assumes zero correlation or independence among the variables because correlation describes a degree of mathematical association not a causal relationship between the two variables. The details of fitting distribution are presented in Appendix. For example, the optimal fitted distribution established by A-D test and graphical methods of body weight variable is showed in Figure 6.1. The input data is represented by bars and the fitted distribution by the line in the plots. The results of input variable distributions used for calculate risks are listed in Table 6.1



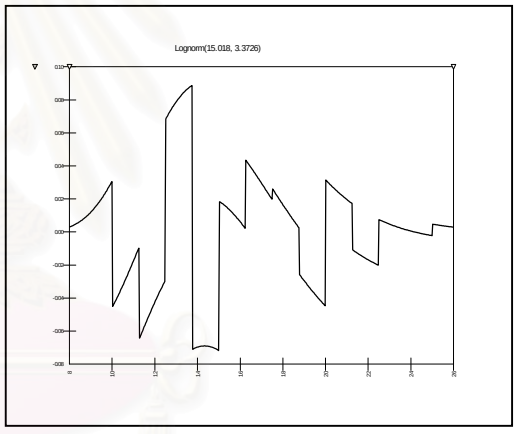
Comparison



P-P plot



Q-Q plot



Difference

Figure 6.1 Distribution and graphic results of body weight

Body weight is described by lognormal distribution with mean 15.018 and standard deviation of 3.37. The distribution of soil ingestion rate was uniform with mean 50 and upper percentile of 175. A triangular distribution of 10-80% of relative bioavailability was selected for absorption factor. Averaging time for noncancer effects is characterized by uniform distribution (200, 2190). A triangular distribution with minimum, mean, and the 95th percentile was used to represent uncertainty in exposure duration. Averaging time for cancer effects, reference dose, and cancer slope factor are represented by point estimates.

Table 6.1 Distribution parameters used in the health risk assessment

Input variable	Symbol	Unit	Distribution
Arsenic concentration in soil	Cs	mg/kg	Lognormal (227.12, 340.37)
Soil ingestion rate	SIR	mg/d	Uniform (50, 175)
Absorption factor	AF	-	Triangular (0.1, 0.2, 0.8)
Body weight	BW	kg	Lognormal (15.018, 3.37)
Exposure duration	ED	years	Uniform(1, 6)
Exposure frequency	EF	days/year	Triangular(200, 350, 365)
Averaging time for noncancer effect	ATnc	days	Uniform (200,2190)
Averaging time for cancer effect	ATc	days	25,550
Conversion factor	CF	kg/mg	1.0E-06
Reference dose	RfD	mg/kg/d	0.0003
Cancer slope factor	CSF	$(mg/kg/d)^{-1}$	1.5

6.2.3 Model Simulation

In the probabilistic approach, inputs to the risk equation are described as random variables that can be defined mathematically by a probability distribution function (PDF). PDF describe the range of values that a variable may assume and indicate the relative likelihood of each value occurring within that range for the exposure population. After determining appropriate PDF types and parameter values

for selected variables, the set of PDFs is combined with the toxicity value in the exposure and risk equations given in equation to estimate a distribution of risks. The following 3 steps were carried out:

(1) Probability distribution (PDF) for each input variable was characterized and the distribution was specified for the MC simulation.

(2) For each iteration of the simulation, one value was randomly selected from each input variable distribution and risk equation was run. Many iterations are performed such that the random selections for each parameter.

(3) The output risks were rendered as probability risk values and cumulative probability plots.

The distributions described above were used in a MC simulation. The @RISK software was used to run the simulation. The simulation was run with 10,000 iterations of the model using Latin Hypercube sampling (LHS) and the results used to estimate various percentiles of risk using the standard risk equation, reference dose, and the cancer slope factor for arsenic. LHS is a stratified sampling scheme that may reach faster convergence over the whole range of the output distributions. These setting were sufficient to obtain stability of <1% difference in the 95^{th} percentile risk estimate. Finally, sensitivity analysis was performed using the Spearman's rank correlation coefficient performed with @RISK software. The parameters are ranked in accordance with the magnitude of effect the parameters are having on model predictions.

It is important to note that model intended to estimate risk from continuous exposure to contaminant may not be appropriate for estimating risk from acute of subchronic exposure events.

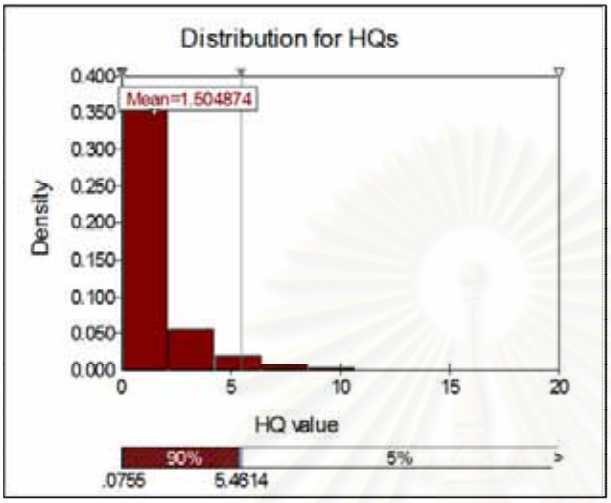
6.2.4 Results

U.S.EPA suggests that 50^{th} percentile of risk should be considered CTE estimate, and 95^{th} percentile of risk may be considered RME estimate. Thus, the same percentiles were chosen in this study. Outputs from the model are distributions describing the HQ and CR. A table of the outputs recorded is given in Table 6.2. Risk plots derived from MC simulations are shown in Figure 6.2 and 6.3. Lifetime cancer risk from soil intake had a 50^{th} percentile of 1.6×10^{-5} and 1.08×10^{-4} for 95^{th} percentile. HQ for children exposed arsenic from soil ingestion were 0.73 and 5.46 based on 50^{th} percentile and 95^{th} percentile, respectively.

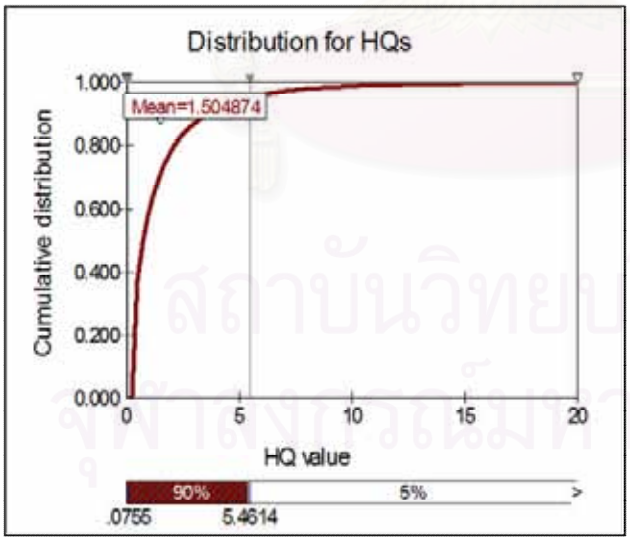
Table 6.2 HQ and CR outputs from soil intake in children

Statistical value	HQ	CR
Min	0.0023	6.06E-08
Mean	1.50	3.06E-05
SD	2.40	4.19E-05
P5	0.08	1.81E-06
P25	0.29	6.66E-06
P50	0.73	1.60E-05
P60	1.01	2.20E-05
P75	1.74	3.71E-05
P90	3.63	7.51E-05
P95	5.46	1.08E-04

P = percentiles

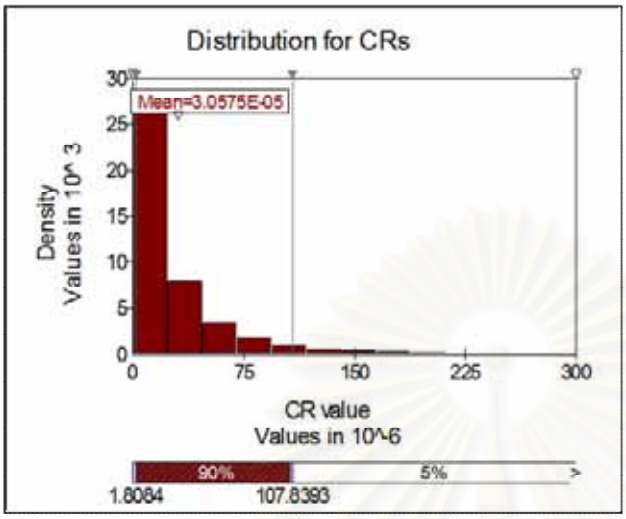


Summary Information	
Workbook Name	children.xls
Number of Simulations	1
Number of Iterations	10000
Number of Inputs	7
Number of Outputs	2
Sampling Type	Latin Hypercube
Simulation Start Time	25/09/2008 11:58
Simulation Stop Time	25/09/2008 11:58
Simulation Duration	00:00:04
Random Seed	932712636

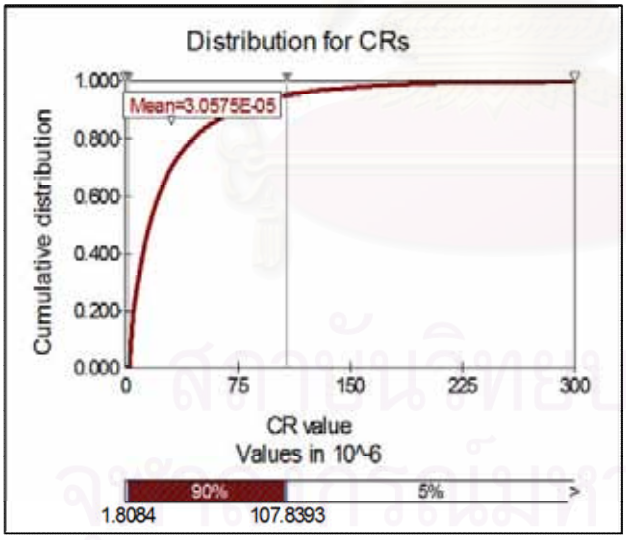


Summary Statistics			
Statistic	Value	%tile	Value
Minimum	0.002310081	5%	0.075477816
Maximum	27.15358734	10%	0.127695844
Mean	1.504874142	15%	0.180905953
Std Dev	2.39884906	20%	0.236925498
Variance	5.754476811	25%	0.293112785
Skewness	5.744076112	30%	0.358734131
Kurtosis	44.37103165	35%	0.436213613
Median	0.732808948	40%	0.521742284
Mode	0.15199301	45%	0.616576672
Left X	0.075477816	50%	0.732808948
Left P	5%	55%	0.853913009
Right X	5.461418629	60%	1.006795168
Right P	95%	65%	1.206392169
Diff X	5.385940813	70%	1.452626228
Diff P	90%	75%	1.735443354
#Errors	0	80%	2.127372265
Filter Min		85%	2.6707201
Filter Max		90%	3.633066654
#Filtered	0	95%	5.461418629

Figure 6.2 Cumulative distribution of HQ from soil intake in children



Summary Information	
Workbook Name	children.xls
Number of Simulations	1
Number of Iterations	10000
Number of Inputs	7
Number of Outputs	2
Sampling Type	Latin Hypercube
Simulation Start Time	25/09/2008 11:58
Simulation Stop Time	25/09/2008 11:58
Simulation Duration	00:00:04
Random Seed	932712636



Summary Statistics			
Statistic	Value	%tile	Value
Minimum	6.05926E-08	5%	1.80844E-06
Maximum	0.00051865	10%	2.93176E-06
Mean	3.0575E-05	15%	4.12755E-06
Std Dev	4.18922E-05	20%	5.36785E-06
Variance	1.75496E-09	25%	6.65638E-06
Skewness	3.617380013	30%	8.18823E-06
Kurtosis	23.34960574	35%	9.76141E-06
Median	1.60298E-05	40%	1.16595E-05
Mode	2.3641E-06	45%	1.36461E-05
Left X	1.80844E-06	50%	1.60298E-05
Left P	5%	55%	1.88402E-05
Right X	0.000107839	60%	2.20316E-05
Right P	95%	65%	2.59762E-05
Diff X	0.000106031	70%	3.05525E-05
Diff P	90%	75%	3.70985E-05
#Errors	0	80%	4.54137E-05
Filter Min		85%	5.65254E-05
Filter Max		90%	7.51112E-05
#Filtered	0	95%	0.000107839

Figure 6.3 Cumulative distribution of CR from soil intake in children

A sensitivity analysis was subsequently conducted to provide a measure of the most important factors affecting the risk to human health from individual arsenic in soil. This information was displayed on a bar chart and can be seen in Figure 6.4 and 6.5. The sensitivity analysis may be the important result of the risk assessment. It can be used to identify factors for which risk management strategies can be based in order to reduce the overall exposure to arsenic. Rank order correlation determines the correlation between input variables and outputs. The correlation coefficient lies between -1 (direct negative correlation) and +1 (direct positive correlation). Correlation values in the vicinity of zero indicate a weak predictive value of the variable. The results of sensitivity analysis are presented in Table 6.3.

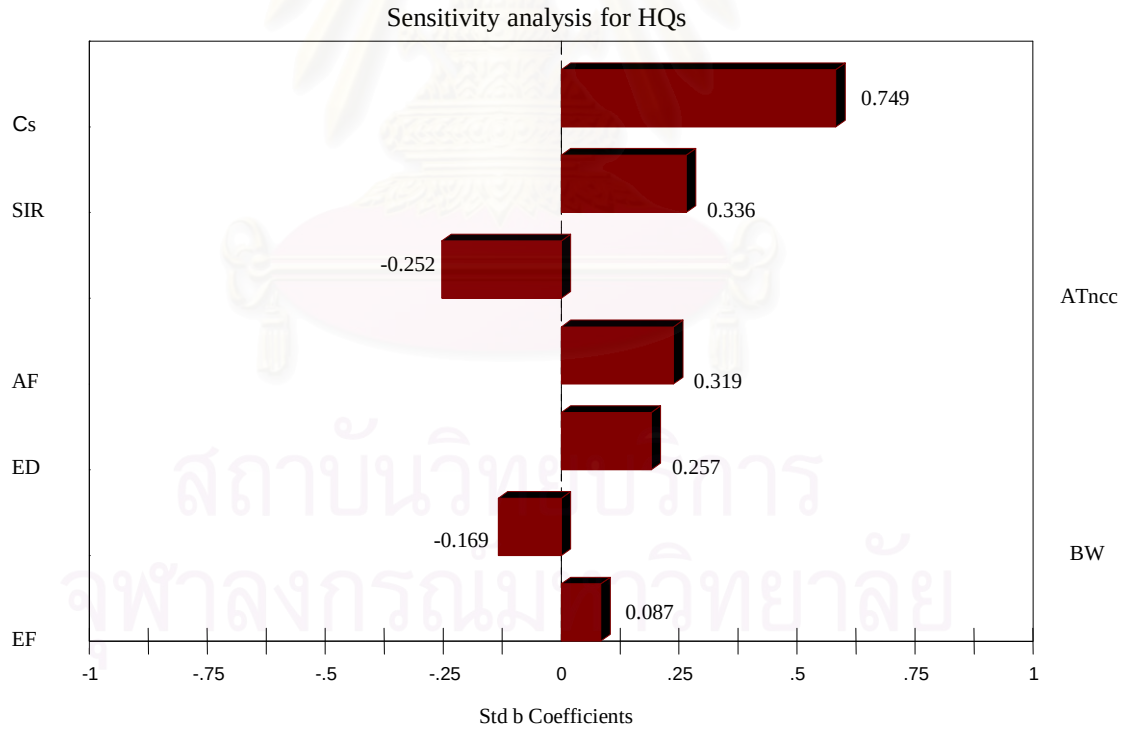


Figure 6.4 Sensitivity analysis of HQ from soil intake in children (HQs)

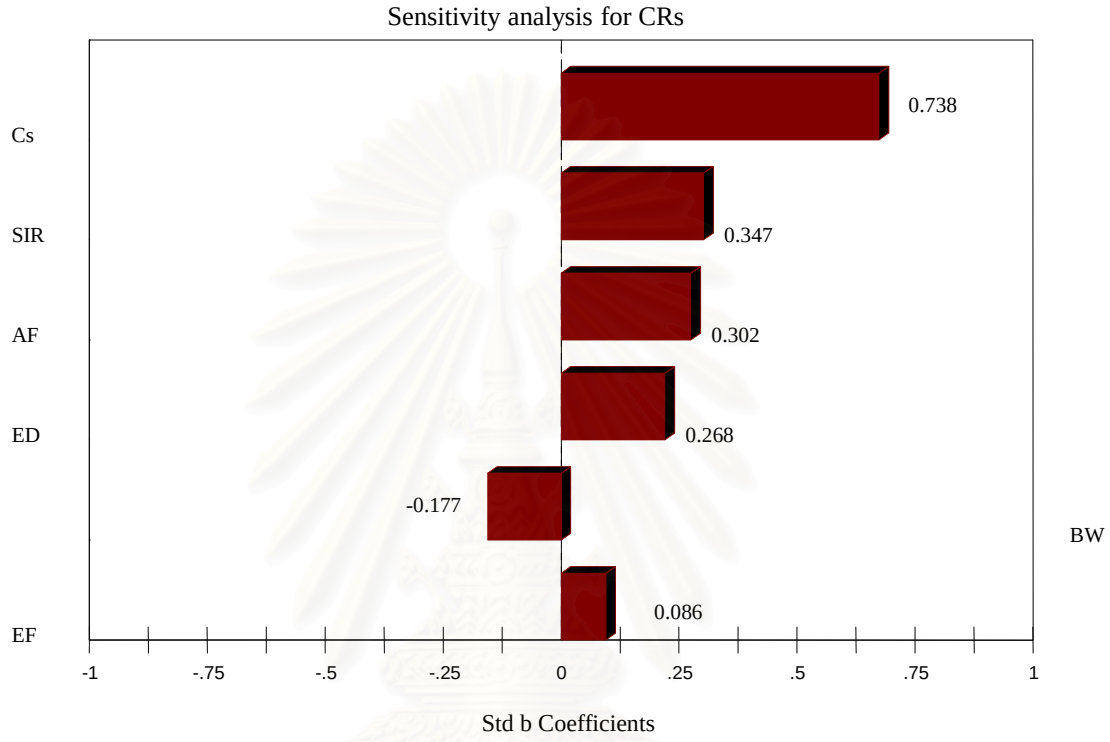


Figure 6.5 Sensitivity analysis of CR from soil intake in children (CRs)

Sensitivity analysis for HQ indicated the three most influential exposure factors were arsenic concentration in soil (59.60%), soil ingestion rate (11.99%), and absorption factor (10.81%). The sensitivity analysis for CR had similar results of HQ, indicating that the amount of arsenic concentration in soil was the most influential parameter (65.55%). Exposure frequency was relatively uninfluential in both risk outputs (0.08%). Table 6.3 summarizes the outputs of sensitivity analysis.

Table 6.3 Sensitivity analysis for risk characterization

Exposure factor	Symbol	Rank correlation value*			
		HQs	Normalized r^2 x 100% for HQsa	CRs	Normalized r^2 x 100% for HQsa
Concentration in soil	Cs	0.749	59.60	0.783	65.55
Soil ingestion rate	SIR	0.336	11.99	0.347	12.87
Absorption factor	AF	0.319	10.81	0.302	9.75
Exposure duration	ED	0.257	7.02	0.268	7.68
Exposure frequency	EF	0.087	0.80	0.086	0.79
Body weight	BW	-0.169	3.03	-.177	3.35
Averaging time for noncancer effects	ATnc	-0.252	6.75	-	-

*@RISK output includes Spearman rank correlation, r, and normalized r^2 values, calculated by dividing each r^2 value by the sum of all r^2 values.

6.2.5 Discussion

The DRA and PRA approaches were slightly difference results of risk. The PRA analysis gave a risk estimate approximately an order of magnitude less than DRA. This decrease is due to the incorporation of probability distribution for input variables that decreases with Monte Carlo method. Comparison between DRA and PRA outputs of HQ and CR are presented in Table 6.4. Deterministic estimates of risk may be not always agrees with probabilistic methods. However, the results of DRA and PRA in this study were similar due to the exposure factors slightly varied with the target population.

Table 6.4 HQ and CR from DRA and PRA from soil intake in children

Method	HQ		CR	
	DRA	PRA	DRA	PRA
CTE	0.32	0.73	4.14×10^{-6}	1.60×10^{-5}
RME	3.62	5.46	1.40×10^{-4}	1.08×10^{-4}

CTE = central tendency estimate; RME = reasonable maximum estimate; DRA = deterministic risk assessment; PRA = probabilistic risk assessment; HQ = hazard quotient; CR = cancer risk

The sensitivity analysis for both HQ and CR had similar results, indicating that the amount of arsenic concentration in soil was the most influential parameter. The identification of influential input variables is an important part of PRA. A sensitivity analysis may also simplify the assessment process if less influential input variables are substituted by point estimates. The assessment work can then be focused on developing reliable probability distributions for the remaining variables. Monte Carlo of LHS simulation is better suited to studying the impact from several input variables together with statistical evaluation. The Spearman rank correlation coefficient is less sensitive to departures from the normal distribution and is therefore often used to evaluate the correlation between the input variables and the outcome. Generally, one would expect the Spearman's rank correlation coefficient for body weight and averaging time to be negative because these factors appear in the denominator of the risk equation (Cullen and Frey, 1999; U.S.EPA, 2001a).

Advantages of MCA outputs provide more information than deterministic point estimate calculations. Distribution functions for the exposure or risk estimate display the ranges of exposure or risk and the probability associated with each value of exposure or risk. Thus, it is possible to determine that a particular risk or exposure level represents the 50^{th}, 90^{th}, 95^{th} percentile or any other percentile level of risk, to

select a level of exposure or risk that corresponds to the desired level of protection. The RME represents the highest exposure reasonably likely to occur. When using PRA, the risk manager can select the RME from the high end range of percentiles of risk, generally between the 90^{th} and 99^{th} percentiles. However, PRA may not be appropriate for every site. Disadvantages of PRA are that it generally requires more time, resources, and expertise on the part of assessor, and reviewer than a point estimate approach. There may be instances where a probabilistic Monte Carlo analysis for various reasons is not an option. For instance, when it is not expected to improve a risk assessment, when the risk is well below concern, when neither time nor resources are available, when the problem can be managed at a low cost anyway, or when rare events have a large impact on the risk. In many other situations, probabilistic Monte Carlo analysis may be useful, e.g. when conservative point estimates fall above levels of concern, in order to rank exposure sources, exposure pathways or contaminants, or when costs are high or the consequences of not managing the problem are unacceptable. In practice, a tiered approach beginning with a simple screening model and progressing to more sophisticated and realistic models may often be the preferred approach (U.S.EPA, 1994, 1997a, 2000a, 2001a).

The risk assessment of substances comprises exposure assessment and effect assessment. Human limit values such as RfD or CSF is the result of an effect assessment (hazard characterization) and is considered to be safe for the general population. The impact of arsenic metabolism and toxicity has been controversial because the risk assessment process used by the U.S.EPA to establish the standard for arsenic is based primarily on dose–response information from poorly fed populations and high consumption rate of water in Taiwan. It has been hypothesized that the Taiwanese populations were particularly susceptible to the health impacts of arsenic (NRC, 2001; U.S.EPA, 1988). These limit values are based on toxicological data and considerations. They are generally derived by using worst case assumptions regarding potential differences between humans, as well as regarding the variability in sensitivity within the general population. Next, product limits may be derived in combination with information on human exposure. From these results, RfD or CSF may was higher level than actually general population of toxic dose. To date,

probabilistic models have more often used for exposure assessment than for toxicity assessment. The current policy is not intended to apply to doe-response evaluations for health risk assessment until this application of probabilistic analysis has been studied further. Future studies should therefore give more attention to uncertainty in the toxicity assessment (Jager et al., 2000; NRC, 2001; U.S.EPA, 1994).

Ideally validation would involve multiple comparisons between model outputs and real data. This study, the validation of the outputs of risk was compared with the current cancer records from National Cancer Institute, Thailand. The estimated lifetime cancer risk for arsenic is 1.0×10^{-4} (1 in 10,000). This means that if 10,000 people were exposed to arsenic in soil at the concentration, frequency and duration of exposure assumed in the calculation detailed in previously Section, there would be a theoretical increase of 1 cancer above the number of cancers that would normally be expected to occur in the population of 10,000. Background rate of cancer in the Thailand is 277:100,000 of population (NCI, 2007) or 27.8:10,000 of population. Arsenic exposures could result in a theoretical increase of 1 cancer case above the background number of 27.2 cancer cases. This represents a relatively low increased cancer risk.

In conclusion, based on the best available information degrading exposure and toxicity, the estimated distribution in risk across the target population was about 95% of individuals exposed under these circumstances have not a cancer risk exceeding 1.0×10^{-4}. However, approximately 40% may be exceeded the safety risk for noncancer effects.

6.3 Risk Characterization of Arsenic from Duplicate Meal and Soil Intake in Adults

6.3.1 Methods

This section describes the equations used to estimate risk via each route of exposure and the data distribution characteristics for each exposure variable. For the purposes of this evaluation, only adults group is considered. Tables 6.5 and 6.6 summarize the data distribution characteristics for soil and duplicate meal exposure variables considered in this analysis, respectively. The software @RISK was used for fitting distribution by the same children methods in the previous Section. The details of fitting distribution are presented in Appendix.

Risk characterizations of arsenic via soil ingestion (HQsa and CRsa) are described by the equation 4.2 and 4.3, state again as:

$$HQsa = \frac{(C \times SIR \times AF \times ED \times EF \times CF)}{(BW \times ATnc)} \times \frac{1}{RfD}$$

$$CRsa = \frac{(C \times SIR \times AF \times ED \times EF \times CF)}{(BW \times ATc)} \times CSF$$

where:

HQsa = hazard quotient from soil intake in adults

CRsa = cancer risk from soil intake in adults

Cs = concentration of arsenic in soil (mg/kg)

AF = absorption factor (unitless)

SIR = soil ingestion rate (mg/d)

CF = a conversion factor of 10^{-6} (kg/mg)

BW = body weight (kg)

AT = averaging time (days), equal to the life expectancy (70 x 365 25,550 days) for carcinogen (ATc), and equal to ED x 365 for noncancer estimation (ATnc)

RfD = reference dose for inorganic arsenic, 0.0003 mg/kg/d

CSF = cancer slope factor for inorganic arsenic, 1.5 per mg/kg/d

Table 6.5 Distribution parameters used in risk characterization from soil intake

Input variable	Symbol	Unit	Distribution
Arsenic concentration in soil	Cs	mg/kg	Lognormal (227.12, 340.37)
Soil ingestion rate	SIR	mg/d	Uniform (35, 120)
Absorption factor	AF	-	Triangular (0.1, 0.2, 0.8)
Body weight	BW	kg	Lognormal (248.07,9.9919)
Exposure duration	ED	years	Extvalue (19.623, 10.37)
Exposure frequency	EF	days/year	Triangular(200, 350, 365)
Averaging time for noncancer effect	ATnc	days	Lonormal (14245, 6678.7)
Averaging time for cancer effect	ATc	days	25,550
Conversion factor	CF	kg/mg	1.0E-06
Reference dose	RfD	mg/kg/d	0.0003
Cancer slope factor	CSF	$(mg/kg/d)^{-1}$	1.5

Body weight is described by lognormal distribution with mean 248.07 and standard deviation of 9.99. The distribution of soil ingestion rate was uniform with ranges 35 and 120 mg/d. A triangular distribution of 0.1, 0.2, 0.8 of relative bioavailability were used for absorption factor. Averaging time for noncancer effects is characterized by lognormal distribution (14245, 6678.7). A triangular distribution with minimum, mean, and the 95^{th} percentile was used to exposure duration variable. Averaging time for cancer effects, reference dose, and cancer slope factor are represented by point estimates. Total soil intake of arsenic in adults included soil expose in children with parameters in Table 6.1.

Inorganic arsenic intake from duplicate meal pathway was estimated by the following equation:

$$HQm = \frac{(Cm \times IR \times AF \times ED \times EF)}{(BW \times ATnc)} \times \frac{1}{RfD}$$

$$CRm = \frac{(Cm \times IR \times AF \times ED \times EF)}{(BW \times ATc)} \times CSF$$

where:

HQm = hazard quotient from duplicate meal intake in adults

CRm = cancer risk from duplicate meal intake in adults

Cm = concentration of arsenic in duplicate meal (mg/g)

IRm = intake rate of duplicate meal (g/d, dry weight)

ED = exposure duration (years)

EF = exposure frequency (day/year)

AF = absorption factor, unitless (AF = 1)

BW = body weight (kg)

AT = averaging time (days), equal to the life expectancy (70 x 365 = 25,550 days) for carcinogen (ATc), and equal to ED x 365 for noncancer estimation (ATnc).

RfD = reference dose for inorganic arsenic, 0.0003 mg/kg/d

CSF = cancer slope factor for inorganic arsenic, per 1.5 mg/kg/d

In duplicate meal analysis, the concentration of arsenic is assigned a normal distribution with mean 0.298 and standard deviation 0.06 mg/g. The distribution of intake rate was lognormal with mean 62.56 and standard deviation 40.99 g/d. Other factors are listed in Table 6.6.

Table 6.6 Distribution parameters used in risk characterization from duplicate meal consumption

Input variable	Symbol	Unit	Distribution
Arsenic concentration in meal	Cm	mg/g	Normal (0.298,0.06)
Intake rate of meal	IRm	g/d	Lognormal (62.56,40.99)
Absorption factor	AF	-	1
Body weight	BW	kg	Lognormal (248.07,9.9919)
Exposure duration	ED	years	Extvalue (19.623, 10.37)
Exposure frequency	EF	days/year	Triangular(200, 350, 365)
Averaging time for noncancer effect	ATnc	days	Lognormal (14245, 6678.7)
Averaging time for cancer effect	ATc	days	25,550
Reference dose	RfD	mg/kg/d	0.0003
Cancer slope factor	CSF	$(mg/kg/d)^{-1}$	1.5

6.3.2 Results and Discussion

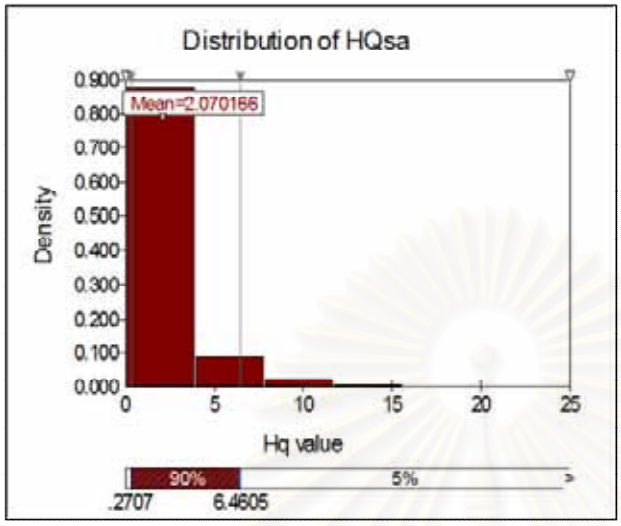
6.3.2.1 Soil intake

Using the @RISK program, the plausible uptake and associated increased cancer risk and hazard quotient were calculated for each exposure pathway. Table 6.7 summarizes the probability distribution of HQsa and CRsa for adults exposed arsenic from soil. CRsa from soil intake had a 50^{th} percentile of 4.8×10^{-5} and 1.53×10^{-4} for the 95^{th} percentile. HQsa for adults exposed arsenic from soil ingestion were 1.22 and 6.46 based on the 50^{th} percentile and the 95^{th} percentile, respectively. Risk plots derived from MC simulations are showed in Figure 6.6 and 6.7.

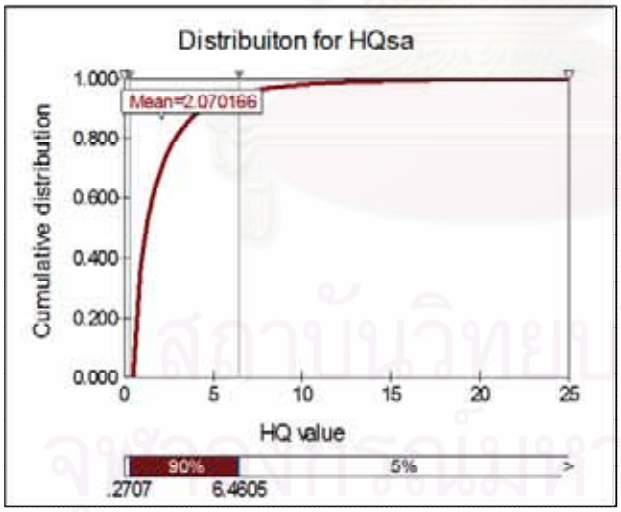
Table 6.7 HQsa and CRsa outputs from soil intake in adults

Statistical value	HQsa	CRsa
Min	0.04	3.14E-06
Mean	2.07	5.98E-05
SD	2.9	4.52E-05
P5	0.27	1.47E-05
P25	0.66	2.99E-05
P50	1.22	4.80E-05
P75	2.4	7.63E-05
P95	6.46	1.53E-04

P = percentiles

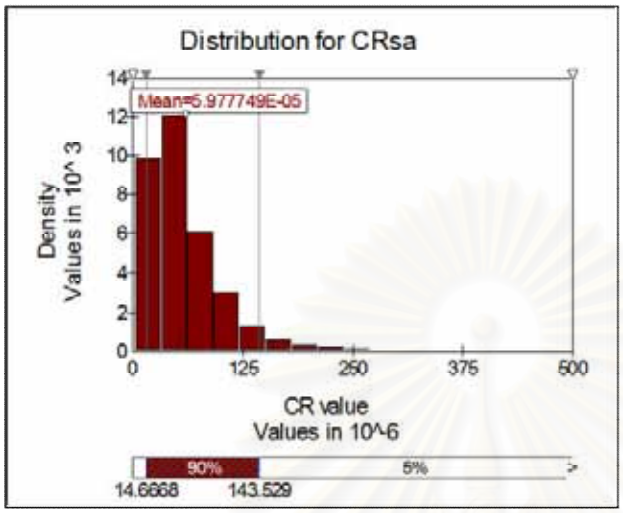


Summary Information	
Workbook Name	Adult.xls
Number of Simulations	1
Number of Iterations	10000
Number of Inputs	12
Number of Outputs	2
Sampling Type	Latin Hypercube
Simulation Start Time	25/10/2008 13:45
Simulation Stop Time	25/10/2008 13:45
Simulation Duration	00:00:04
Random Seed	1229908019

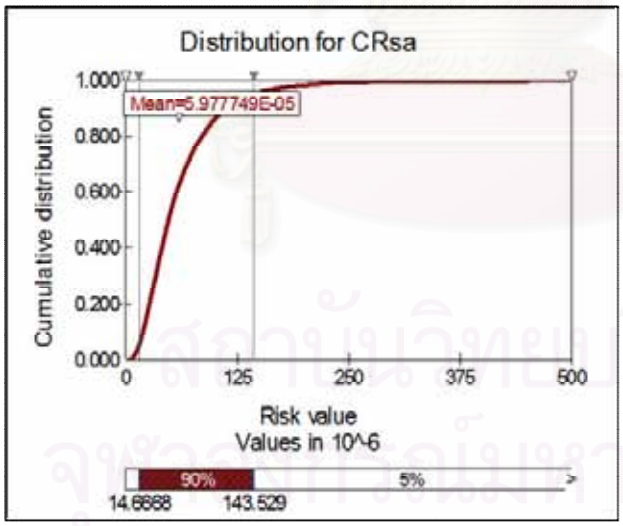


Summary Statistics			
Statistic	Value	%tile	Value
Minimum	0.044727977	5%	0.270705014
Maximum	85.63780212	10%	0.371822417
Mean	2.070166185	15%	0.46533221
Std Dev	2.903633333	20%	0.558468759
Variance	8.431086534	25%	0.65596652
Skewness	7.781578321	30%	0.752124727
Kurtosis	136.4793903	35%	0.854700863
Median	1.215498567	40%	0.964608073
Mode	0.566175541	45%	1.089011073
Left X	0.270705014	50%	1.215498567
Left P	5%	55%	1.380468249
Right X	6.460465908	60%	1.559907198
Right P	95%	65%	1.785543442
Diff X	6.189760894	70%	2.055631876
Diff P	90%	75%	2.403532028
#Errors	0	80%	2.871007442
Filter Min		85%	3.491381168
Filter Max		90%	4.441243172
#Filtered	0	95%	6.460465908

Figure 6.6 Cumulative distribution of HQsa from soil intake in adults



Summary Information	
Workbook Name	Adult.xls
Number of Simulations	1
Number of Iterations	10000
Number of Inputs	12
Number of Outputs	2
Sampling Type	Latin Hypercube
Simulation Start Time	25/10/2008 14:15
Simulation Stop Time	25/10/2008 14:15
Simulation Duration	00:00:04
Random Seed	1229908019



Summary Statistics			
Statistic	Value	%tile	Value
Minimum	3.14277E-06	5%	1.46668E-05
Maximum	0.000655928	10%	1.92012E-05
Mean	5.97775E-05	15%	2.30269E-05
Std Dev	4.51768E-05	20%	2.65686E-05
Variance	2.04094E-09	25%	2.98916E-05
Skewness	2.581217835	30%	3.34007E-05
Kurtosis	16.40227508	35%	3.68419E-05
Median	4.79576E-05	40%	4.0294E-05
Mode	3.76924E-05	45%	4.40727E-05
Left X	1.46668E-05	50%	4.79576E-05
Left P	5%	55%	5.22115E-05
Right X	0.000153529	60%	5.6906E-05
Right P	95%	65%	6.24449E-05
Diff X	0.000138862	70%	6.88198E-05
Diff P	90%	75%	7.63394E-05
#Errors	0	80%	8.57111E-05
Filter Min		85%	9.70914E-05
Filter Max		90%	0.000112427
#Filtered	0	95%	0.000153529

Figure 6.7 Cumulative distribution of CRsa from soil intake in adults

Comparison of the HQ and CR results between DRA and PRA approaches are presented in Table 6.8. The DRA and PRA results were slightly different from the results of risk. The PRA analysis gave a risk estimate approximately an order of magnitude less than DRA. The difference is due to the incorporation of probability distribution for input variables with Monte Carlo method. HQ from DRA were 0.38 (CTE) and 4.24 (RME) while PRA for the same exposure situation the 50^{th} percentile was 1.22 and the 95^{th} percentile was 6.46. HQ from soil intake in adults both DRA and PRA approaches were higher than acceptable level of HQ = 1. CR level from RME both DRA and PRA ranged 1.53×10^{-4} to 3.7×10^{-4} that it means approximately 2 - 4 in 10,000 population probably increased cancer risk.

Table 6.8 HQ and CR from DRA and PRA from soil intake in adults

Statistic value	HQ		CR	
	DRA	PRA	DRA	PRA
CTE	0.38	1.22	1.25×10^{-5}	3.54×10^{-5}
RME	4.24	6.46	3.70×10^{-4}	1.53×10^{-4}

CTE = central tendency estimate; RME = reasonable maximum estimate; DRA = deterministic risk assessment; PRA = probabilistic risk assessment; HQ = hazard quotient; CR = cancer risk

Sensitivity analysis for HQsa (Figure 6.8) indicated the three influential (directive positive correlation) exposure factors were arsenic concentration in soil, exposure duration in children, and soil ingestion rate in children similarity the results of sensitivity analysis in children. The most influential in CRsa (Figure 6.9) was concentration of arsenic and exposure duration in children. Soil ingestion rate was affected of risk than soil ingestion rate in adults. Sensitivity analysis results for risk characterization from soil intake in adults are listed in Table 6.9.

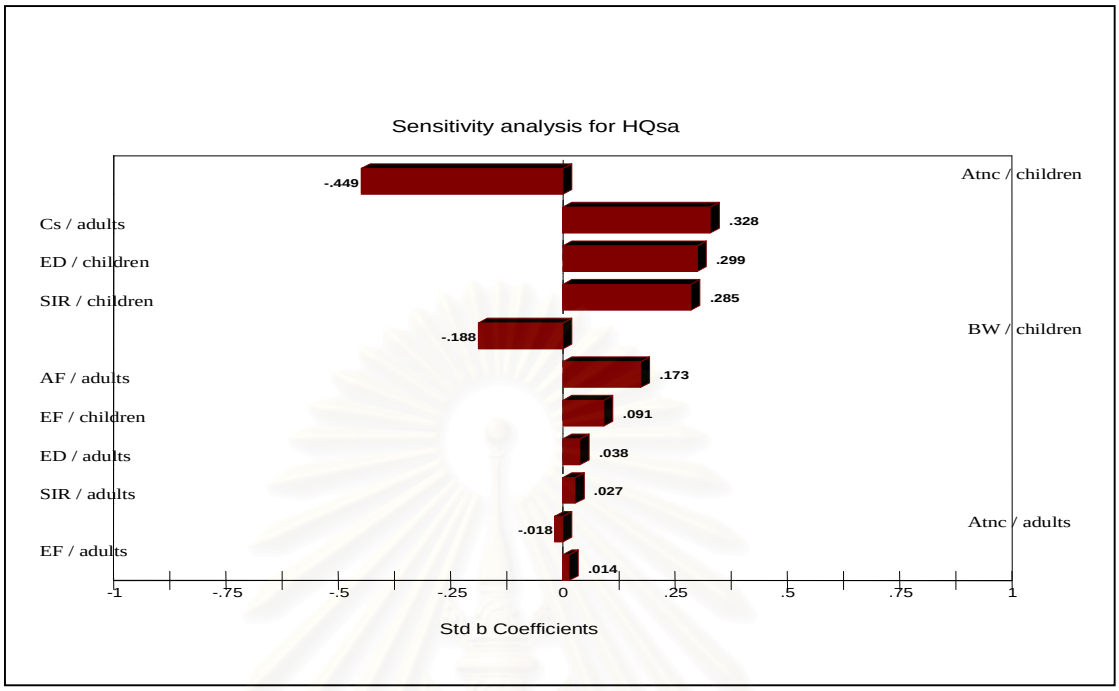


Figure 6.8 Sensitivity analysis of HQ from soil intake in adults (HQsa)

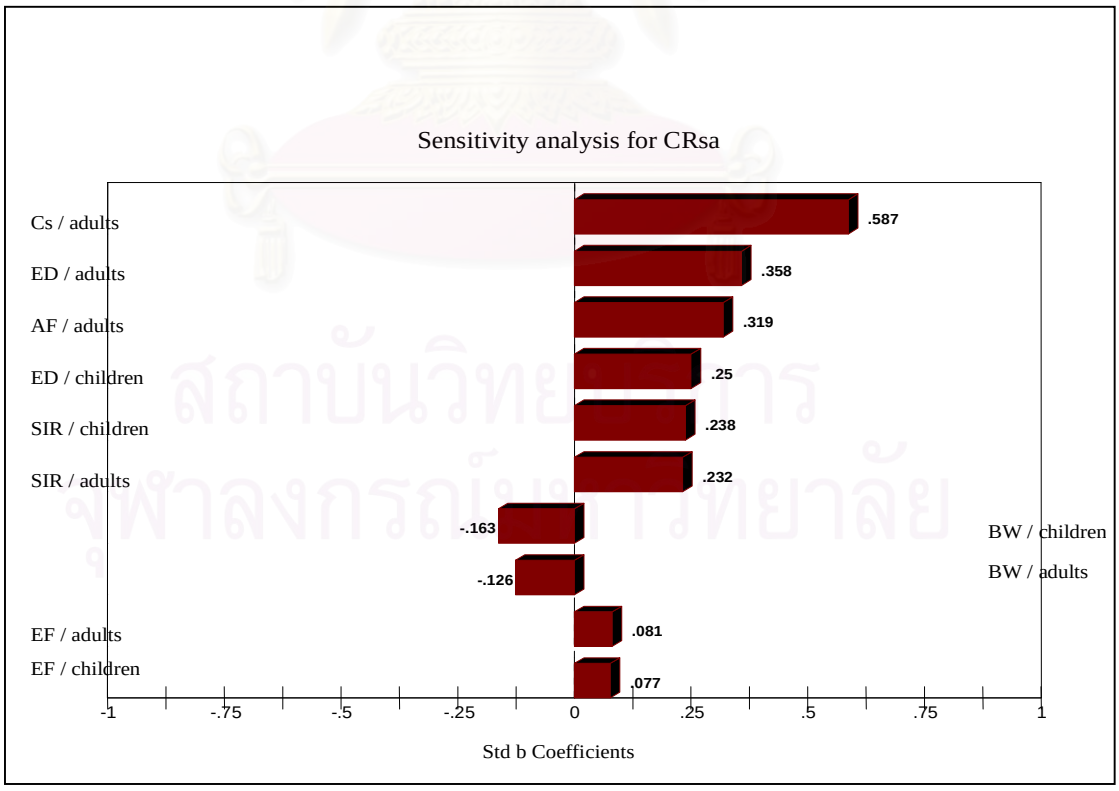


Figure 6.9 Sensitivity analysis of CR from soil intake in adults (CRsa)

Table 6.9 Sensitivity analysis for risk characterization from soil intake in adults

Exposure factor	Symbol	Rank correlation value*			
		HQsa	Normalized r^2 x 100% for HQsa	CRsa	Normalized r^2 x 100% for HQsa
Exposure duration in adults	ED/adults	.038	0.26	.358	15.97
Exposure duration in children	ED/children	.299	16.08	.25	7.79
Concentration in soil	Cs	.328	19.35	.587	42.44
Absorption factor	AF	.173	5.38	.319	12.68
Soil ingestion rate in adults	SIR/adults	.027	0.13	.232	6.7
Soil ingestion rate in children	SIR/children	.285	14.6	.238	7.06
Exposure frequency in adults	EF/adults	.014	0.03	.081	0.81
Exposure frequency in children	EF/children	.091	1.5	.077	0.74
Averaging time for noncancer, adults	ATnc/adults	-.018	0.06	-	-
Averaging time for noncancer, children	ATnc/children	-.449	36.25	-	-
Body weight, adults	BW/adults	.000	0	-.126	1.97
Body weight, children	BW/children	-.188	6.35	-.163	3.31

*@RISK output includes Spearman rank correlation, r, and normalized r^2 values, calculated by dividing each r^2 value by the sum of all r^2 values.

Conclusion in this part, HQ greater than 1 indicated that exposure arsenic from soil intake in adults was likely to result in noncancer effects. While, the 95th percentile of cancer risk from PRA was 1.53 x 10^{-4} that means about 2 in 10,000 people may be increased cancer effect from the background. Although, normally adults ingested soil was lower than children but they spent of longer time of exposure. Thus in this study, the majority influential of cancer risk level in adults from soil intake were arsenic concentration and exposure duration.

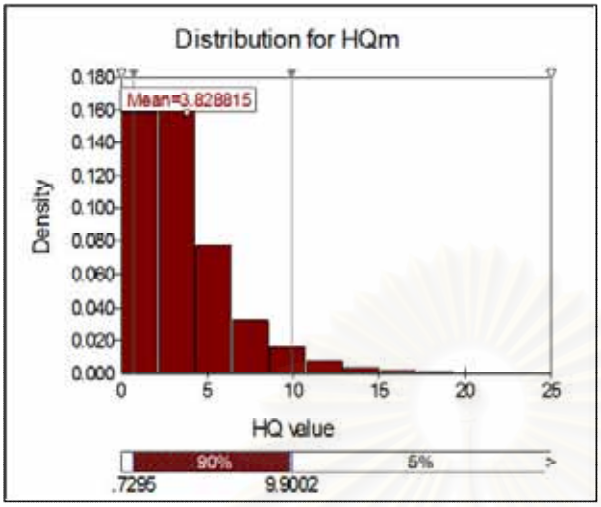
6.3.2.2 Duplicate meal intake

Table 6.10 summarizes the probability distribution of HQm and CRm for adults. CRm had the 50th percentile of 6.76 x 10^{-4} and 1.74 x 10^{-3} for the 95th percentile. HQm were 2.99 and 9.90 based on the 50th percentile and the 95th percentile, respectively. Risk plots derived from MC simulations are presented in Figure 6.10 and 6.11.

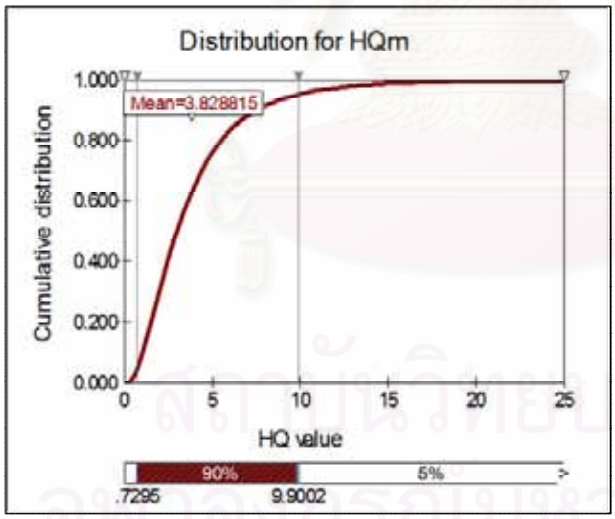
Table 6.10 HQm and CRm outputs in adults

Statistical value	HQ	CR
Min	0.01	2.75E-06
Mean	3.83	7.92E-04
SD	3.19	5.07E-04
P5	0.73	2.12E-04
P10	1.03	2.80E-04
P25	1.75	4.40E-04
P50	2.99	6.76E-04
P75	4.89	1.01E-03
P95	9.90	1.74E-03

P = percentiles

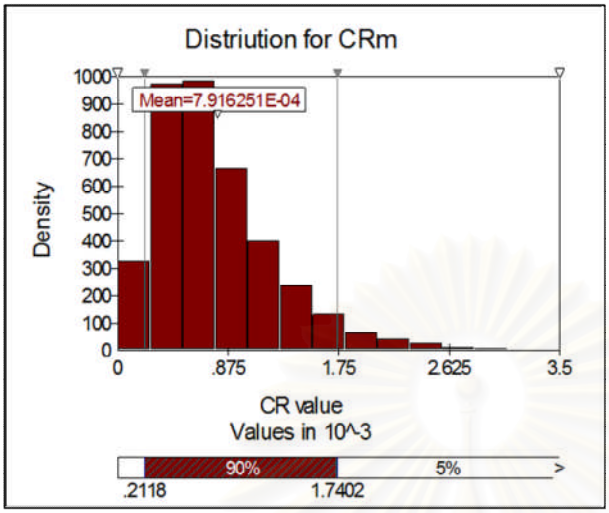


Summary Information	
Workbook Name	Adult.xls
Number of Simulations	1
Number of Iterations	10000
Number of Inputs	9
Number of Outputs	2
Sampling Type	Latin Hypercube
Simulation Start Time	25/10/2008 16:45
Simulation Stop Time	25/10/2008 16:45
Simulation Duration	00:00:04
Random Seed	20593796

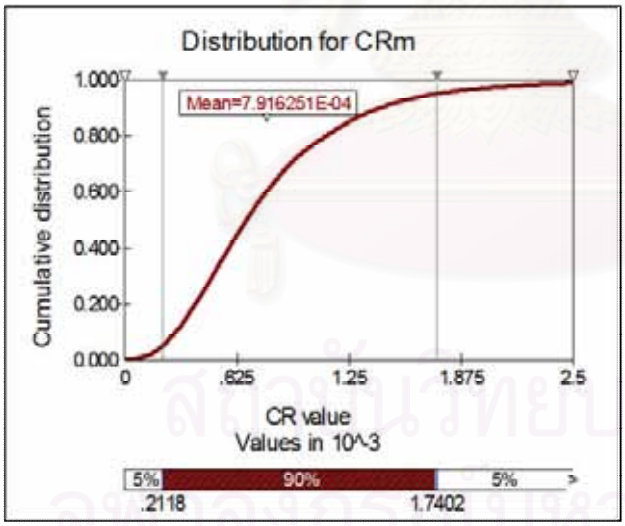


Summary Statistics			
Statistic	Value	%tile	Value
Minimum	0.011468645	5%	0.729460001
Maximum	47.3772049	10%	1.038457632
Mean	3.828815427	15%	1.281247139
Std Dev	3.197449987	20%	1.514821172
Variance	10.22368642	25%	1.748796105
Skewness	2.752714225	30%	1.981388688
Kurtosis	17.83301267	35%	2.202296019
Median	2.989702225	40%	2.444057703
Mode	1.819175651	45%	2.690072298
Left X	0.729460001	50%	2.989702225
Left P	5%	55%	3.288780451
Right X	9.900200844	60%	3.631064653
Right P	95%	65%	3.983644485
Diff X	9.170740843	70%	4.414132118
Diff P	90%	75%	4.889733315
#Errors	0	80%	5.505322933
Filter Min		85%	6.30678463
Filter Max		90%	7.540302753
#Filtered	0	95%	9.900200844

Figure 6.10 Cumulative distribution of HQm



Summary Information	
Workbook Name	Adult.xls
Number of Simulations	1
Number of Iterations	10000
Number of Inputs	9
Number of Outputs	2
Sampling Type	Latin Hypercube
Simulation Start Time	25/10/2008 16:45
Simulation Stop Time	25/10/2008 16:45
Simulation Duration	00:00:04
Random Seed	20593796



Summary Statistics			
Statistic	Value	%tile	Value
Minimum	2.7527E-06	5%	0.000211766
Maximum	0.005659549	10%	0.00028035
Mean	0.000791625	15%	0.000339702
Std Dev	0.000509382	20%	0.000393926
Variance	2.5947E-07	25%	0.000441509
Skewness	1.790669754	30%	0.000486649
Kurtosis	8.95437931	35%	0.000532363
Median	0.00067609	40%	0.00057936
Mode	0.00039734	45%	0.000626785
Left X	0.000211766	50%	0.00067609
Left P	5%	55%	0.000730593
Right X	0.001740168	60%	0.000791107
Right P	95%	65%	0.000853274
Diff X	0.001528402	70%	0.000925775
Diff P	90%	75%	0.001014385
#Errors	0	80%	0.001126386
Filter Min		85%	0.001255508
Filter Max		90%	0.001437643
#Filtered	0	95%	0.001740168

Figure 6.11 Cumulative distribution of CRm

Comparison of the HQm and CRm results between DRA and PRA approaches are presented in Table 6.11. The DRA and PRA results were slightly different results of risk. Cancer risk from PRA was below DRA approach and the confidence interval of risk from CTE and RME was lower than DRA. However, both DRA and PRA methods were risk level higher than acceptable value of HQ = 1 and CR = 1.0×10^{-4}. Approximately 7 in 10,000 to 2 in 1,000 of people who expose arsenic via duplicate meal may be increased cancer risk when estimated by PRA. Similarity the results from DRA method but the upper percentile of cancer risk from DRA was higher.

Table 6.11 HQm and CRm from DRA and PRA from duplicate meal intake in adults

Method	HQm		CRm	
	DRA	PRA	DRA	PRA
CTE	5.33	2.99	9.00×10^{-4}	6.76×10^{-4}
RME	9.00	9.90	3.60×10^{-3}	1.74×10^{-3}

CTE = central tendency estimate; RME = reasonable maximum estimate; DRA = deterministic risk assessment; PRA = probabilistic risk assessment; HQm = hazard quotient from duplicate meal pathway; CRm = cancer risk from duplicate meal pathway.

The results of sensitivity analysis indicated that all exposure variables (ED, EF, and AT) impacted greatly on the risk estimate (about 80%). Figure 6.12 - 6.13, and Table 6.12 shows the sensitivity results of risk from duplicate meal exposure.

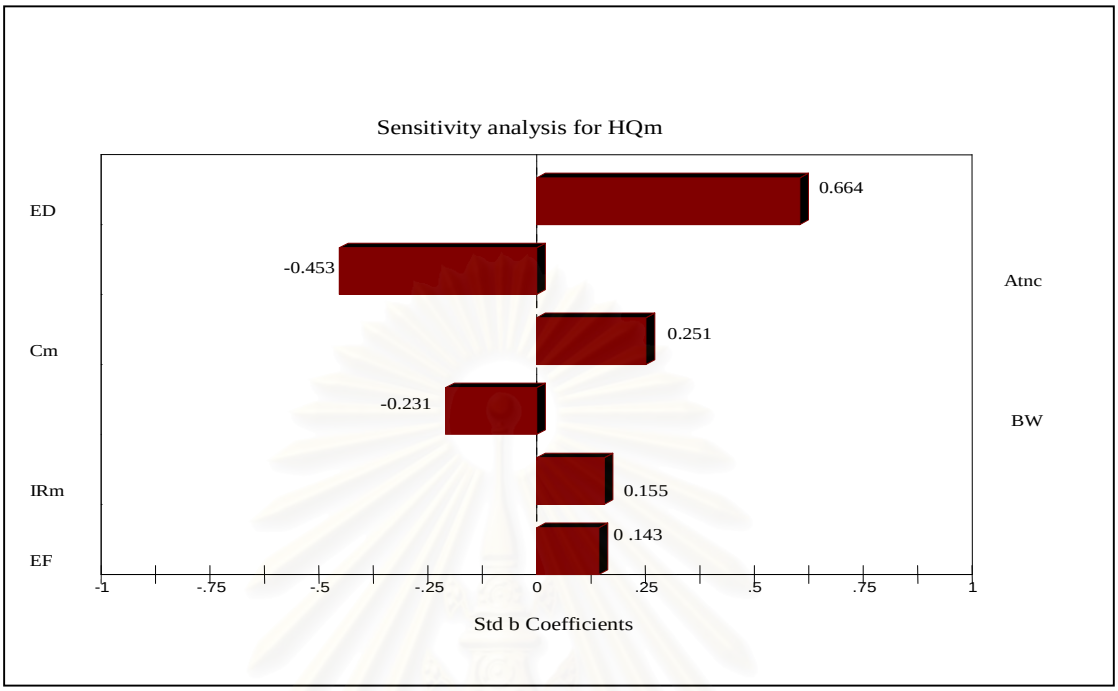


Figure 6.12 Sensitivity analysis of HQ from duplicate meal intake in adults (HQm)

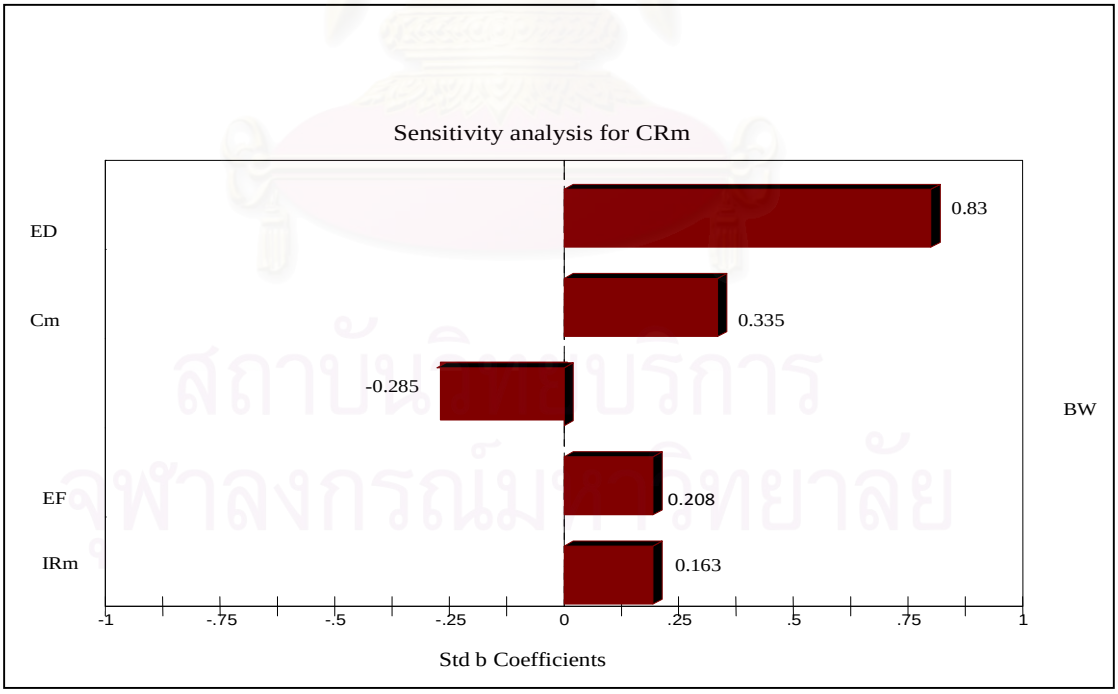


Figure 6.13 Sensitivity analysis of CR from duplicate meal intake in adults (CRm)

Table 6.12 Sensitivity analysis for risk characterization from duplicate meal intake

Exposure factor	Symbol	Rank correlation value*			
		HQm	Normalized r^2 x 100% for HQm	CRm	Normalized r^2 x 100% for CRm
Exposure duration	ED	0.664	54.64	0.830	72.35
Concentration in meal	Cm	0.251	7.81	0.335	11.79
Ingestion rate	IRm	0.155	2.98	0.163	2.79
Exposure frequency	EF	0.143	2.53	0.208	4.54
Averaging time for noncancer effects	ATnc	-0.453	25.43	-	-
Body weight	BW	-0.231	6.61	-.285	8.53

*@RISK output includes Spearman rank correlation, r, and normalized r^2 values, calculated by dividing each r^2 value by the sum of all r^2 values.

6.3.2.3 Total risk estimate in adults

The total increased cancer risk (TCR) and hazard quotient (in term hazard index, HI) for each pathway were calculated as follows:

$$HI = HQsa + HQm$$

$$TCR = CRsa + CRm$$

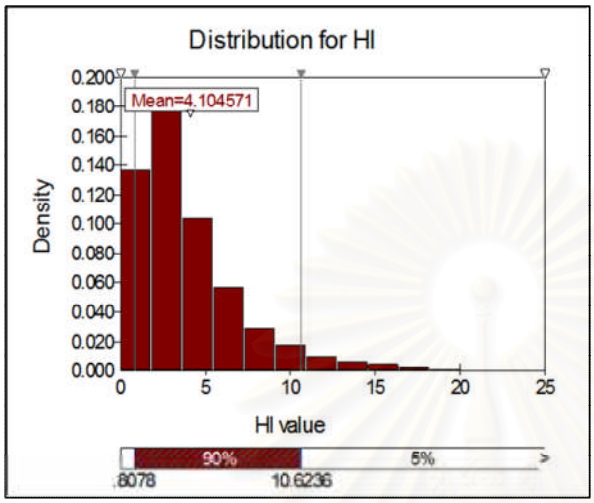
Table 6.13 summarizes the total increased cancer risk at the 50^{th} percentile was 7.25×10^{-4} and the 95^{th} percentile increased risk was 1.83×10^{-3}. Soil ingestion rate for estimate total risk is described by uniform (50,120) and other factors were the

same parameters for calculate risk of soil exposure in adults. Figure 6.14 and 6.15 shows the cumulative distribution of HI and TCR.

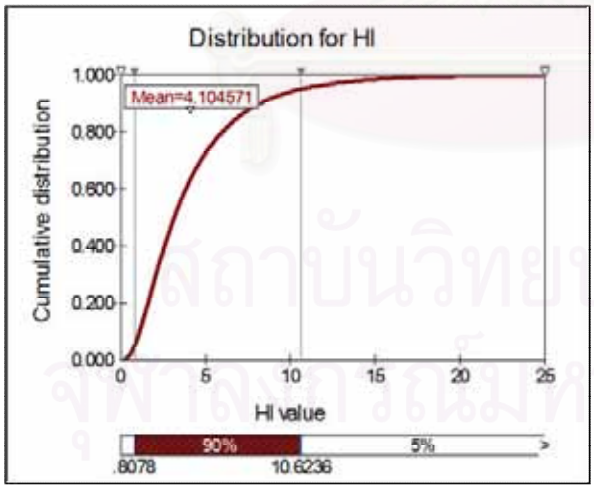
Table 6.13 HI and TCR in adults

Statistic value	HI	TCR
Min	0.02	4.23E-06
Mean	4.10	8.42E-04
SD	3.40	5.34E-04
P5	0.81	2.27E-04
P10	1.10	3.08E-04
P25	1.84	4.70E-04
P50	3.16	7.25E-04
P75	5.28	1.09E-03
P95	10.62	1.83E-03

P = percentiles

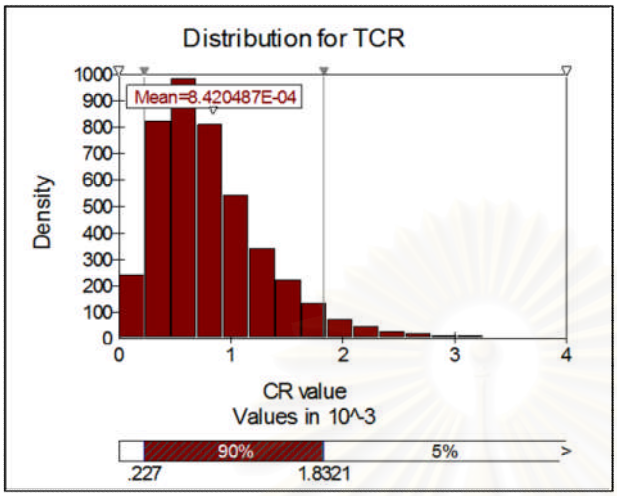


Summary Information	
Workbook Name	Adult.xls
Number of Simulations	1
Number of Iterations	10000
Number of Inputs	9
Number of Outputs	2
Sampling Type	Latin Hypercube
Simulation Start Time	25/10/2008 17:04
Simulation Stop Time	25/10/2008 17:04
Simulation Duration	00:00:04
Random Seed	2096851710

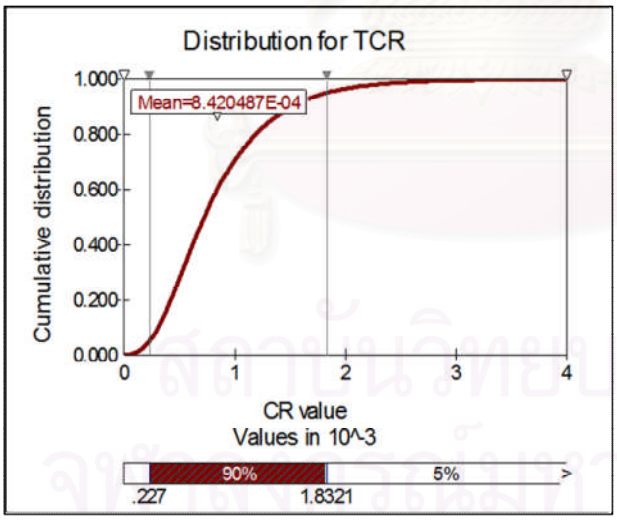


Summary Statistics			
Statistic	Value	%tile	Value
Minimum	0.018533152	5%	0.807847023
Maximum	40.09976578	10%	1.102034926
Mean	4.104570758	15%	1.362032175
Std Dev	3.401957924	20%	1.612783074
Variance	11.57331771	25%	1.843183756
Skewness	2.377201484	30%	2.082600832
Kurtosis	12.70922758	35%	2.316411972
Median	3.157110453	40%	2.584278584
Mode	1.825749053	45%	2.853622198
Left X	0.807847023	50%	3.157110453
Left P	5%	55%	3.471463203
Right X	10.62355232	60%	3.844688654
Right P	95%	65%	4.236922741
Diff X	9.815705299	70%	4.712449074
Diff P	90%	75%	5.280884266
#Errors	0	80%	5.980470181
Filter Min		85%	6.889075756
Filter Max		90%	8.210528374
#Filtered	0	95%	10.62355232

Figure 6.14 Cumulative distribution of HI



Summary Information	
Workbook Name	Adult.xls
Number of Simulations	1
Number of Iterations	10000
Number of Inputs	9
Number of Outputs	2
Sampling Type	Latin Hypercube
Simulation Start Time	25/10/2008 17:04
Simulation Stop Time	25/10/2008 17:04
Simulation Duration	00:00:04
Random Seed	2096851710



Summary Statistics			
Statistic	Value	%tile	Value
Minimum	4.23189E-06	5%	0.000227015
Maximum	0.005126932	10%	0.000308493
Mean	0.000842049	15%	0.000368927
Std Dev	0.000530466	20%	0.000420187
Variance	2.81395E-07	25%	0.00047201
Skewness	1.678276092	30%	0.000522924
Kurtosis	7.999927668	35%	0.000570393
Median	0.000724886	40%	0.000619008
Mode	0.000720597	45%	0.000670401
Left X	0.000227015	50%	0.000724886
Left P	5%	55%	0.000781388
Right X	0.001832107	60%	0.000839829
Right P	95%	65%	0.000909045
Diff X	0.001605092	70%	0.000993031
Diff P	90%	75%	0.001086343
#Errors	0	80%	0.001187667
Filter Min		85%	0.00132801
Filter Max		90%	0.001516833
#Filtered	0	95%	0.001832107

Figure 6.15 Cumulative distribution of TCR

Sensitivity analysis of HI and TCR indicated the most influential of risk estimates were exposure variables (includes ED, ET, and ATnc) and arsenic concentration in duplicate meal. Approximately 80% of influence on risk resulted from all exposure factors and about 10% from concentration of arsenic. Table 6.14 lists all variables of calculate risk and results when testing by sensitivity analysis and these results are showed in Figure 6.16 and 6.17.

Table 6.14 Sensitivity analysis for HI and TCR

Exposure factor	Symbol	Rank correlation value*			
		HI	Normalized r^2 x 100% for HI	TCR	Normalized r^2 x 100% for TCR
Exposure duration	ED	0.679	48.99	0.841	75.14
Concentration in meal	Cm	0.253	6.80	0.317	10.68
Exposure frequency	EF	0.156	2.59	0.196	4.08
Ingestion rate of meal	IRm	0.116	2.17	0.143	2.17
Absorption factor	AF	0.045	0.22	0.040	0.17
Concentration in soil	Cs	0.036	0.14	0.036	0.14
Soil ingestion rate	SIR	0.026	0.07	0.031	0.10
Averaging time for noncancer effects	ATnc	-0.572	34.76	-	-
Body weight	BW	-0.217	5.00	0.266	7.52

*@RISK output includes Spearman rank correlation, r, and normalized r^2 values, calculated by dividing each r^2 value by the sum of all r^2 values.

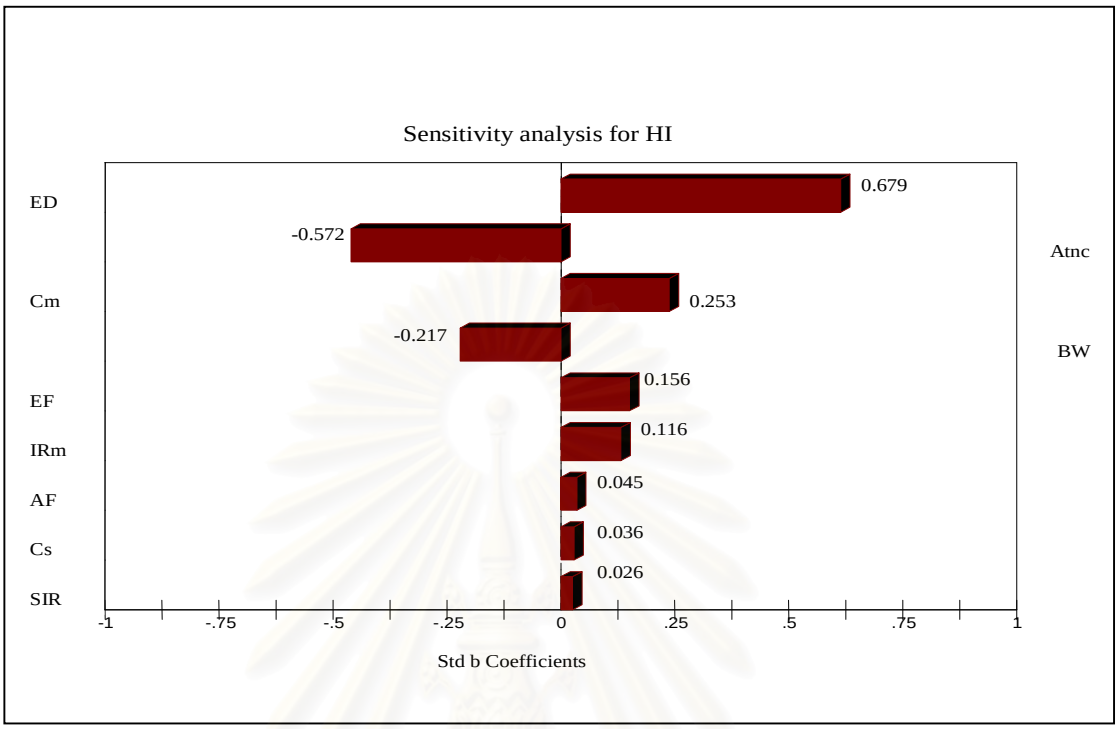


Figure 6.16 Sensitivity analysis of HI

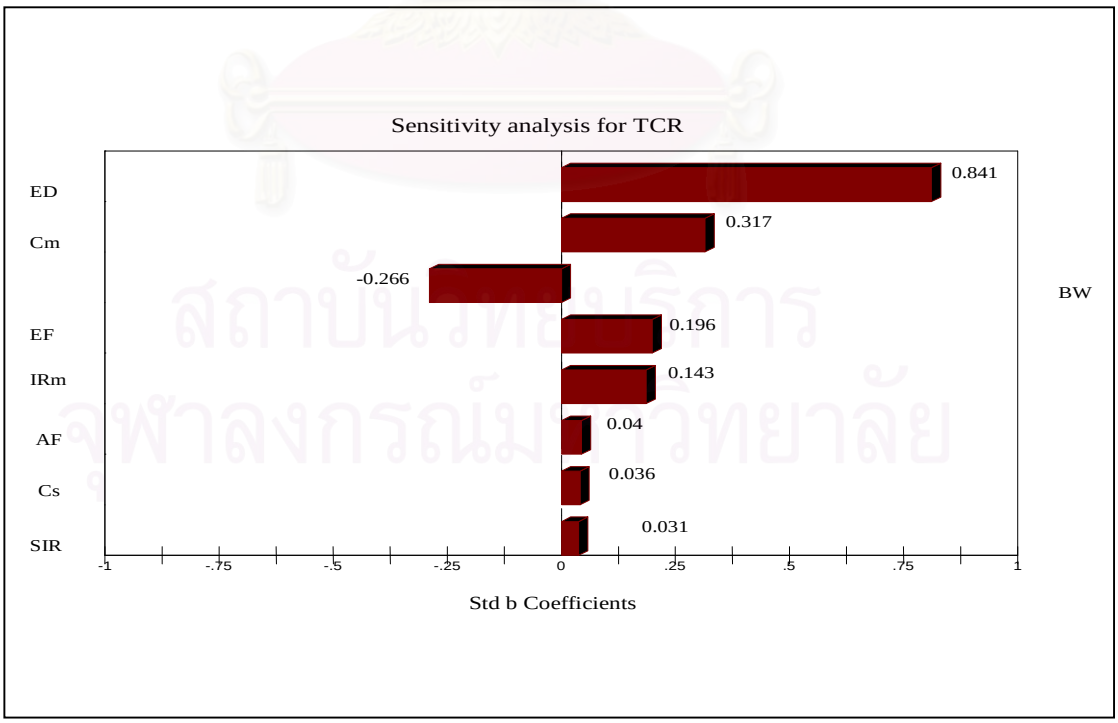


Figure 6.17 Sensitivity analysis of TCR

HI value was slightly different between DRA and PRA approaches and TCR of DRA by using RME estimate was higher than PRA about 3 times because RME in DRA approach used the point of the upper percentiles for calculate risk. However, both DRA and PRA results showed that both noncancer and cancer risk levels were greater than safety risk (Table 6.15).

Table 6.15 Comparison of HI and TCR between DRA and PRA approaches

Method	HI		TCR	
	DRA	PRA	DRA	PRA
CTE	5.71	3.16	9.13×10^{-4}	7.25×10^{-4}
RME	13.24	10.62	3.97×10^{-3}	1.83×10^{-3}

CTE = central tendency estimate; RME = reasonable maximum estimate; DRA = deterministic risk assessment; PRA = probabilistic risk assessment

In conclusions, arsenic in duplicate meal related human health risks are of serious concern in Ronphibun, the 50^{th} percentile of lifetime cancer risk from meal of 6.76×10^{-4} and 1.74×10^{-3} based on the 95^{th} percentile level being calculated for the population in this study, was higher than the 1.0×10^{-4} typically threshold values. The 50^{th} percentile of total cancer risk from combined meal and soil intake was 7.25×10^{-4} and 1.83×10^{-3} as the 95^{th} percentile that means if 1,000 people were exposed to arsenic in soil and duplicate meal at the concentration, frequency and duration of exposure assumed in the calculation, there would be a theoretical increase of 1.83 cancer above the number of cancers that would normally be expected to occur in the population of 1,000. If background rate of cancer in the Thailand is 277:100,000 of population (NCI, 2007) or 2.77:1,000 of population that arsenic exposures could result in a theoretical increase of 1.83 cancer case above the background number of 2.77 cancer cases. This represents a high increased cancer risk. Based on the best available information degrading exposure and toxicity, the estimated distribution in

risk across the target population in the present study was more than 95% of individuals exposed under these circumstances have a cancer risk exceeding 1.0×10^{-4} and about 90% may be exceeded the safety risk for noncancer effects (HI = 1).

Sensitivity analysis of HI and TCR indicated the most influential of risk estimates were exposure variables and arsenic concentration in duplicate meal. Approximately 80% of influence on risk resulted from all duration factors and about 10% from concentration of arsenic in duplicate meal. The contributions to risks from meal and soil pathway were found to be 88% and 12%, respectively. Meal is a major potential source of arsenic exposure in the arsenic affected study area in Ronphibun. However, it is difficult to separate and specify the types of food and raw materials intake in this study because the replicate meal sampling was used for the purpose of actual intake and decrease varies of cooking method.

Most studies to date have used fist order Monte Carlo simulation. The method is relatively simple to understand and is convenient due to the availability of commercial software (Cullen and Frey, 1999; Ferton, 1996). The question for the policy maker now becomes, “What level of risk is acceptable?”. This more complex assessment will not simplify the decision because the decision is dependent on many factors such as economic factors, social factors, political factors, legal factors, technological factors and public value. In this case, each of the factors is given a weighting on move people to safety land or cleanup soil because the majority of risk was resulted from a longer exposure time and higher level arsenic in soil that it can transferred to food and water.

The proposed PRA for health effect can not be validated directly because there exists no instrument that can measure probabilistic risk. Note that the same can be said about the conventional, deterministic risk assessment. However, it is possible to validate components or steps of PRA. But since the main goal of this thesis is to estimate risk only the techniques were validated by Monte Carlo simulation in commercial @RISK software. The underlying risk assessments principles as for example using soil intake as a way to set standards and protect human is not studied here.

The information to describe the shape of the dose-response curve for exposure induced adverse effects in humans due to inorganic arsenic and its biological metabolites has not been adequately developed to support a scientifically defensible mode of action. Inorganic arsenic is a human carcinogen based on epidemiological evidence. To determine the dose of arsenic related to cancer in an exposed population, U.S.EPA (1988) has used a linearized multistage model which assumes that extrapolation from high doses to low doses is possible with a straight line and at low doses the slope of the dose–response curve is represented by a slope factor. The report carcinogenic effects in population with decades of exposure to concentrations of inorganic arsenic on the order of several hundred ppb in drinking water. NRC and U.S.EPA concluded that the data from Taiwan were the most appropriate data sets to estimate cancer risk for US population. RfD and CSF for inorganic arsenic may be over an order of magnitude higher than actually value. However, the dose-response assessment of inorganic arsenic has yet to be elucidated and is difficult to determine solely from the available epidemiological studies because the absence of sufficient data to describe a biologically plausible and scientifically defensible mode of action (U.S.EPA, 2000c).

The limited database on the bioconcentration factor for duplicate meal and dose–response relationship in local data has resulted in their general point estimates being entered in the model limiting the variability and uncertainties to be ascertained. The bioavailability of arsenic through food can differ from that via drinking water. Unfortunately, data on arsenic absorption via food has not been reported.

CHAPTER VII

SUMMARY AND CONCLUSIONS

The present study was conducted to investigate soil ingestion rate in Thai people, to estimate the risk from exposure to contaminated arsenic in soil both adults and children in Ronphibun district, and to assess total risk in adults from exposure to arsenic by soil ingestion and food consumption by using deterministic and probabilistic risk assessment approaches.

The research procedures were divided into three main parts. First part included the procedures of investigation of soil ingestion in both adults and children. The study of soil ingestion in children and adults was conducted in Patthalung province nearby Ronphibun district. This study used purposive sampling method for collecting samples. Second part, the amounts of arsenic from ingested soil and duplicate meal consumption were used to assess the levels of exposure. The third part, deterministic and probabilistic risk assessments with central tendency and reasonable maximum methods were used to characterize of risk.

The results of research can be summarized as follows;

1. Average of soil ingestion rates in Thai adults were 22.53 to 27.16 mg/d, the 95^{th} percentile of 114.77 to 127.39 mg/d based on three tracer elements. In children, 29.88 to 36.33 mg/d and 157.38 to 190.94 mg/d were of mean and 95^{th} percentile values, respectively.

2. The recommended values were 35 mg/d for a mean and 120 mg/d for upper percentile values of soil ingestion rate for Thai adults. An average and the upper percentile for Thai children were recommended of 50 mg/d and 175 mg/d, respectively.

3. In adults, deterministic risk characterization (DRA) of arsenic from contaminated soil intake were 0.38 and 4.24 for hazard quotient (HQ) and 1.25 x 10^{-5} and 3.7 x 10^{-4} for cancer risk (CR) based on central tendency estimate (CTE) and reasonable maximum estimate (RME), respectively. In duplicate meal analysis, HQ were 5.33 and 9.00 and CR were 9.0 x 10^{-4} and 3.6 x 10^{-3} based on CTE and RME estimates, respectively. Hazard index (HI) and total cancer risks (TCR) were 5.71 and 13.24, and 9.13 x 10^{-4} and 3.97 x 10^{-3} based on CTE and RME of DRA, respectively. PRA of HI and TCR were 3.16 and 10.62, and 7.25 x 10^{-4} and 1.83 x 10^{-3} based on the 50^{th} percentile and the 95^{th} percentile level, respectively.

4. In children, HQ from deterministic risk assessments were 0.32 and 3.62 based on CTE and RME estimates, respectively. HQ from probabilistic risk assessments were 0.73 and 5.46. The CTE and RME of cancer risk from DRA were 4.14 x 10^{-6} and 1.4 x 10^{-4}, respectively and cancer risk from PRA approach were 1.6 x 10^{-5} ad 1.08 x 10^{-4} based on the 50^{th} percentile and the 95^{th} percentile level, respectively.

5. Sensitivity analysis in PRA indicted that a longer exposure of arsenic and higher concentration of arsenic in meal and soil were the most influential of risk estimates.

The difference between the present study and previous studies in Ronphibon district is the use of inorganic arsenic content in duplicate meal rather than total arsenic to estimate risk. Inorganic arsenic is considered to be the most toxic form and currently dose-response assessment is only based on exposure to inorganic arsenic. Arsenic concentration may differ between uncooked and cooked. Duplicate diet studies are considered to be more accurate at estimating personal exposures because they account for the individual food and water source, the type and quantity of food items consumed, cooking method, and the agricultural conditions under which the food is cultivated. It is important to note that the estimates derived from duplicate diet studies depend on the dietary habits of the participants in local area and may not be generalized to other regions.

Typically, U.S.EPA uses deterministic or point risk assessment (DRA) approaches to characterize risk and applies probabilistic risk assessment (PRA) techniques for characterization of risk, usually within exposure assessments. Point estimate risk assessment uses single value to represent variables in a risk equation. A point estimate of risk can be a central tendency exposure (CTE) or reasonable maximum exposure (RME). CTE represents the average or typical individual in a population usually considered to be the mean or median. RME is defined as the highest exposure that is reasonably expected to occur at a site. The high-end of exposure occurs between the 90^{th} - 99^{th} percentiles. The output of deterministic estimation is a point of risk. Since the results of point estimation generally do not lend more characterize of variability and uncertainty to assessors (U.S.EPA, 1989; 2000a; 2001a). Risk characterizations are influenced by both the variability and uncertainty in the exposure and dose-response assessments. Quantitative probabilistic modeling techniques such as Monte Carlo analysis can be used to incorporate and evaluate sources of variability and uncertainty in risk assessment and the use of these tools is becoming common practice in most health risk evaluations.

PRA is a risk assessment that yields a probability distribution for risk, generally by assigning a probability distribution to represent variability and uncertainty in one or more inputs to the risk equation. Risk estimates are calculated using probability based techniques such as Monte Carlo analysis and can be presented as an entire probability distribution or selected percentiles. An important advantage of probabilistic risk assessments is that it permits to consider the whole distribution of exposure. In this way, more meaningful information is provided to risk managers and public. A second important advantage is the possibility to carry out a sensitivity analysis (U.S.EPA, 1994, 1995b, 1997d, 2001a; Vose, 2000). However, for some area the additional information provided by PRA will not affect the decision that would have been made with a point estimate approach alone and PRA will not be useful.

Cullen and Frey (1999) suggested that probabilistic analysis is useful when a screening level analysis indicates that exposure and risk may be unacceptably high, there is a need to identify priorities for collecting additional information in an effort to reduce uncertainty, significant equity issues are raised regarding the inter-individual

distribution of exposure and risk, there is a need to identify, and determine how to target resources to reduce risk to particular subpopulations of highly exposed individuals, there is a need to rank exposures, pathways, sites, or contaminants taking into account both variability and uncertainty, and when the cost of remediation or intervention is high. Conversely, probabilistic analysis may not be needed in situations where a conservative screening analysis indicates no significant problem or when the costs of intervention or remediation are sufficiently small that they outweigh the costs of analysis. Another possible but unlikely reason that a probabilistic analysis might not be needed is if the variability and uncertainty are sufficiently narrow that a single point estimate is considered to be reliable. However, if in area is a need to identify uncertainty and variability, U.S.EPA has advised the risk assessor to distinguish between variability and uncertainty. Uncertainty represents a lack of knowledge about factors affecting exposure or risk, whereas variability arises from true heterogeneity across people, places, or time. In other words, uncertainty can lead to inaccurate or biased estimates, whereas variability can affect the precision of the estimates and the degree to which they can be generalized (U.S.EPA, 1997c, 1997d, 2000a, 2000b).

Previously risk assessment studies in food and soil intake from adults in Ronphibun area was calculated by DRA or point estimate of risk. However, the results are slightly different from DRA and PRA in the present study and all results of risk were increased than the acceptable risk both noncarcer and cancer effects. Thus, the study of risk from exposure arsenic in this site from the present study, other researches, and governmental agencies may be sufficient for making decision to solve the problem. However, the resolution of this crisis is succeeded or not that depend on the corporative responsibility of people who living in this area.

From the results of HQ and CR that were higher level than acceptable risk values while average daily dose (ADD) and lifetime average daily dose (LADD) were lower than regulatory standard of Thai, WHO (PTDI), ATSDR (acuteMRL). High risk levels were may be resulted from dose-response values both reference dose (RfD) and cancer slope factor (CSF). RfD and CSF were generated by Taiwanese data, many agencies and scientists suggested that the results of HQ and CR may be higher

level than general population exposure when current RfD and CSF are used. Thus, before risk manager made a decision to solve the problem should be attended to this factor. If possible, each arsenic affected area should be evaluated dose-response relationship by using local epidemiological data. In addition, the suggestion for future studies could be as follows: economic of public health assessment and planning for uses of land for prevent the spread of arsenic to widely environment.

REFERENCES

Agency for Toxic Substances and Disease Registry (ATSDR). 2005. Public health assessment guidance manual. Agency for Toxic Substances and Disease Registry, U.S. Department of Health and Human Services.

Agency for Toxic Substances and Disease Registry (ATSDR). 2007. Toxicological profile for arsenic. Agency for Toxic Substances and Disease Registry, U.S. Department of Health and Human Services.

Ahmad, S.A., Bandaranayake, D., and Khan, A.W. 1997. Arsenic contamination in ground water and arsenicosis in Bangladesh. Int. J. Environ. Health Res. 7(4) :271-276.

Ahsan, H., Chen, Y., Parvez, F., et al. 2006. Arsenic exposure from drinking water and risk of premalignant skin lesions in Bangladesh: Baseline results from the health effects of arsenic longitudinal study. Am. J. Epidemiol. 163(12) :1138-1148.

Australian New Zealand Food Authority (ANZFA). The 1994 Australian market basket survey- a total diet survey of pesticides and contaminants[Online]. 1994. Available from: http://www.foodstandardards.gov.au [1994, November 1].

Bae, M., Watanabe, C., and Inaoka, T. 2002. Arsenic in cooked rice in Bangladesh. Lancet 360 :1839–1840.

Baird, S.J.S., Cohen, J.T., Graham, J.D., Shlyakhter, A.J., and Evans, J.S. 1996. Noncancer risk assessment: a probabilistic alternative to current practice. Hum. Eco. Risk Assess. 2 :79-102.

Benramdane, L., Bressolle, F., and Vallon, J.J. 1999. Arsenic speciation in humans and food products: A review. J. Chromatogr. Sci. 37 :330-344.

Binder, S., Sokal, D., and Maughan, D. 1986. Estimating soil ingestion: the use of tracer elements in estimating the amount of soil ingested by young children. Arch Environ Health. 41(6) :341-345.

Binkowitz, B.S., and Wartenberg, D. 2001. Disparity in quantitative risk assessment: A review of input distributions. Risk Anal. 21 :75–90.

Burmaster, D.E., and Anderson, P.D. 1994. Principles of good practice for the use of Monte Carlo techniques in human health and ecological risk assessment. Risk Anal. 14 :477-491.

Calabrese, E.J., and Stanek, E.J. 1991. A guide to interpreting soil ingestion studies: II.Qualitative and quantitative evidence of soil ingestion. Regul. Toxicol. Pharmacol. 13: 278–292.

Calabrese, E.J., Barnes, R., Stanek, E.J., et al. 1989. How much soil do young children ingest: An epidemiologic study. Regul. Toxicol. Pharmacol. 10: 123–137.

Calabrese, E.J., Stanek, E.J., and Barnes, R. 1996. Methodology to estimate the amount and particle size of soil ingested by children: Implications for exposure assessment at waste sites. Regul. Toxicol. Pharmacol. 24: 264-268.

Calabrese, E.J., Stanek, E.J., Gilbert, C.E., and Barnes, R.M. 1990. Preliminary adult soil ingestion estimates: Results of a pilot study. Regul. Toxicol. Pharmacol. 12(1) : 88–95.

Calabrese, E.J., Stanek, E.J., James, R.C., and Roberts, S.M. 1997a. Soil ingestion: a concern for acute toxicity in children. Environ. Health Perspect. 105(12) :1354-1358.

Calabrese, E.J., Stanek, E.J., Pekow, P., and Barnes, R.M. 1997b. Soil ingestion estimates for children residing on a superfund site. Ecotoxicol. Environ. Safe. 36(3) :258-268.

Calderon, R.L., Hudgens, E., and Le, C.X. 1999. Excretion of arsenic in urine as a function of exposure to arsenic in drinking water. Environ. Health Perspect. 107 :663-667.

Califonia Environmental Protection Agency (CalEPA). 2000. Technical support document for exposure assessment and stochastic analysis. Califonia Environmental Protection Agency, USA.

Canadian Council of Ministers of the Environment (CCME). 1997. Canadian soil quality guidelines for the protection of environmental and human health. Canadian Council of Ministers of the Environment, Winnipeg.

Carrington, C.D., and Bolger, P.M. 1998. Uncertainty and risk assessment. Hum. Ecol. Risk Assess. 4: 253-258.

Carrizales, L., Razo, I., Tellez-Hernandez, J.I., et al. 2006. Exposure to arsenic and lead of children living near a copper-smelter in San Luis Potosi, Mexico: importance of soil contamination for exposure of children. Environ. Res. 101: 1-10.

Chan, P.C., and Huff, J. 1997. Arsenic carcinogenesis in animals and in humans: mechanistic, experimental, and epidemiological evidence. J. Environ. Health Sci. 15(2): 83-122.

Chantarawijit, C., Yaowapanon, Y., and Wechcapan, T. 2000. Risk factors and health risk of people in Ronphibun exposed to arsenic. Thai J. Hlth. Promot. Environ. 23(1): 70-78.

Chongsuvivatwong, V., Lim, A., Dueravee, M., Geater, A., Ritsamitchai, S., and Oshikawa, S. 2000. Follow up of water use in a tin mining affected with arsenic poisoning 2000. Southeast Asian J. Trop. Med. Health 31: 769-774.

Choprapawon, C and Rodcline, A. 1997. Chronic arsenic poisoning in Ronphibool, Nakron Sri Thammarat the southern province of Thailand. In Abernathy, C.O., Calderson, R.L., and Chappell, W.R. (eds.), Arsenic exposure and health effects. pp 69-77. Chapman and Hall, London, UK.

Chowdhury, U.K., Rahman, M.M., Mondal, B.K., et al. 2001. Groundwater arsenic contamination and human suffering in West Bengal, India and Bangladesh. Environ. Sci. 8: 393–415.

Clausing, P., Brunekreef, B., and van Wijnen, J.H. 1987. A method for estimating soil ingestion by children. Int. Arch. Occup. Environ. Health 59(1): 73-82.

Concha, G., Nermell, B., and Vahter, M. 1998. Metabolism of inorganic arsenic in children with chronic high arsenic exposure in Northern Argentina. Environ. Health Perspec. 106: 355-359.

Concha, G., Vogler, G., Nermell, B., et al. 2002. Intra-individual variation in the metabolism of inorganic arsenic. Int. Arch. Occup. Enviro.n Health 75 :576-580.

Cullen, W.R., and Frey, H.C. 1999. Probabilistic techniques in exposure assessment: A handbook for dealing with variability and uncertainty in models and inputs. NY: Plenu Press.

Dabeka, R.W., Mckenzie, A.D., Lacroix, G.M.A., et al. 1993. Survey of arsenic in total diet food composites and estimation of the dietary intake of arsenic by Canadian adults and children. J. AOAC Inter. 76: 14-25.

Davis, S., and Mirick. D.K. 2006. Soil ingestion in children and adults in the same family. J. Expo. Sci. Environ. Epidem. 16: 63-75.

Davis, S., Waller, P., Buschom, R., Ballou, J., and White, P. 1990. Quantitative estimates of soil ingestion in normal chilgren between the ages of 2 and 7 years: population-based estimates using aluminum, silicon, and titanium as soil tracer elements. Arch. Environ. Health 45(2): 112-122.

Department of Environment, Food and Rural Affairs and the Environment Agency (DEFRA). 2002. Contaminants in soils: collation of toxicological data and intake values for humans, arsenic. Department of Environment, Food and Rural Affairs and the Environment Agency, Swindon, UK.

Department of Environmental Promotion (DEP). 2002. Final report: Human health risk assessment from exposed to hazards in people living around the landfill at Pathumthani province. Department of Environmental Promotion, Thailand.

Department of Environmental Promotion (DEP). 2005. Final report of evaluation of safety from arsenic exposure in Ronphibun district, Nakhon Si Thammarat province. Department of Environmental Promotion, Thailand.

Department of Medical Science (DMS). 2002. The report of arsenic concentration in food and water. Department of Medical Science, Thailand.

Department of Medical Science (DMS). 2003. The report of risk assessment of arsenic in Ronphibun residents. Department of Medical Science, Thailand.

Devesa, V., Velez, D., and Montoro, R. 2008. Effect of thermal treatments on arsenic species contents in food. Food Chem. Toxicol. 46: 1-8.

Farmer, J.G., and Johnson, L.R. 1990. Assessment of occupational exposure to inorganic arsenic based on urinary concentration and speciation of arsenic. Br. J. Ind. Med. 47: 342-348.

Ferson, S. 1996. What Monte Carlo methods cannot do. Hum. Ecol. Risk Assess. 2: 990-1007.

Finley, B., and Paustenbach, D. 1994. The benefits of probabilistic exposure assessment: Three case studies involving contaminated air, water, and soil. Risk Anal. 53: 54-57.

Fishman, G.S. 2006. A first course in Monte Carlo. Belmont, CA: Thomson Brooks/Cole Press.

Fordyce, F.M., Williams, T.M., Paijitprapapon, A., and Charoenchaisri, P. 1994. Hydrogeochemistry of arsenic in Ronphibun district, Nakhon Si Thammarat province, Thailand. British Geological Survey Oversea Geology Series Technical Report WC/94/79R.

Foy, H.M., Tarmapai, S., Eamchan, P., and Metdilogkul, O. 1992. Chronic arsenic poisoning from well water in a mining area in Thailand. Asia Pac. J. Public. Health 6(3): 150-152.

Frey, H.C., and Rhodes, D.S. 1998. Characterization and simulation of uncertainty frequency distributions: effect of distribution choice, variability, uncertainty, and parameter dependence. Hum. Eco. Risk Assess. 4: 423-469.

Food Standards Agency (FSA). 2004. Total and inorganic arsenic in the 1999 total diet study. Food Standards Agency, London, UK.

Garcia-Manyes, S., Jimenez, G., Padro, A., Rubio, R. and Rauret, G. 2002. Arsenic speciation in contaminated soils. Talanta 58: 97-109.

Graham, J., Berry, M., Bryan, E.F., et al. 1992. The role of exposure databases in risk assessment. Arch. Environ. Health 47: 408-420.

Gunderson, E.L. 1995. FDA total diet study, July 1986-April 1991, dietary intakes of pesticides, selected elements, and other chemicals. J. AOAC Inter. 78: 1353-1363.

Haas, C.N. 1997. Importance of the distributional form in characterizing inputs to Monte Carlo risk assessment. Risk Anal. 17: 107-113.

Hamed, M.M. 2000. Impact of random variables probability distribution on public health risk assessment from contaminated soil. J. Soil Contam. 9: 99–117.

Hattis, D., and Burmaster, D. 1994. Assessment of variability and uncertainty distributions for practical risk analysis. Risk Anal. 14: 713-729.

Haupert, T.A., Wiersma, J.H., and Goldring, J.M. 1996. Health effects of ingesting arsenic-contaminated groundwater. Wis. Med. J. 95(2): 100-104.

Hawley, J.K. 1985. Assessment of health risk from exposure to contaminated soil. Risk Anal. 5: 289-302.

Helgesen, H., and Larsen, E.H. 1998. Bioavailability and speciation of arsenic in carrots grown in contaminated soil. Analyst 123(5): 791-796.

Hazardous Substances Data Bank (HSDB). Arsenic[Online]. 2007. Available from: http://toxnet.nlm.nih.gov [2007, January, 16].

Huang, Y.K., Lin, K.H., Chen, H.W., Chang, C.C., Liu, C.W., Yang, M.H., and Hsueh, Y.M. 2003. Arsenic species contents at aquaculture farm and in farmed mouthbreeder (*Oreochromis mossambicus*) in blackfoot disease hyperendermic areas. Food Chem. Toxicol. 41: 1491-1500.

Hughes, M.F. 2002. Arsenic toxicity and potential mechanisms of action. Toxicol. Lett. 133(1): 1-16.

Hughes, M.F. 2006. Biomarkers of exposure: A case study with inorganic arsenic. Environ. Health Perspect. 114: 1790-1796.

Hwang, Y.H., Bornschein, R.L., Grote, J., Menrath, W., and Roda, S. 1997. Environmental arsenic exposure of children around a former copper smelter site. Environ. Res. 72: 72-81.

Integrated Risk Information System (IRIS). IRIS summary of inorganic arsenic [Online]. 1998. Available from: http://www.cfpub.epa.gov/ncea/iris[1998, April 1].

International Agency for Research on Cancer (IARC). 1980. Arsenic and arsenic compounds. International Agency for Research on Cancer, Lyon, France.

International Programme on Chemical Safety (IPCS). 2001. Environmental Health Criteria: Arsenic and arsenic compounds. International Programme on Chemical Safety. World Health Organization, Geneva.

Jager, T., Hollander, H.A., Janssen, G.B., van der Poel, P., Rikken, M.G.J., and Vermeire, T.G. 2000. Probabilistic risk assessment for new and existing chemicals: Example calculations. RIVM, Bilthoven, the Netherlands.

Jager, T., Vermeire, T.G., Rikken, M.G.J., and van der Poelc, P. 2001. Opportunities for a probabilistic risk assessment of chemicals in the European Union. Chemosphere 43: 257–264.

Japan International Cooperative Agency (JICA). 2000. Final report on the environmental management planning survey for arsenic contaminated area of the Nakhon Si Thammarat province in The Kingdom of Thailand. Japan International Cooperative Agency submitted to Ministry of Science, Technology and Environment, Thailand.

Juhasz, A.l., Smith, E., Weber, J., Rees, M., Rofe, A., Kucher, T., Sansom, L., and Naidu, R. 2006. In vivo assessment of arsenic bioavailability in rice and its significance for human health risk assessment. Environ. Health Perspect. 114: 1826-1831.

Khaokham, D. 2003. Soil ingested by Thai adults between the ages of 20 and 45 years in Pathumthanee. Master's Thesis. Department of Veterinary Public Health, Faculty of Veterinary Science, Chulalongkorn University.

Kile, M.L., Houseman, E.A., Breton, et al. 2007. Dietary arsenic exposure in Bangladesh. Environ. Health Perspect. 115: 889-899.

Kitchin, K.T. 2001. Recent advances in arsenic carcinogenesis: Modes of action, animal model systems, and methylated arsenic metabolites. Toxicol. Appl. Pharmacol. 172(3): 249-261.

Laparra, J.M., Velez, D., Barbera, R., Farre, R., and Montoro, R. 2005. Bioavailability of inorganic arsenic in cooked rice: practical aspects for human health risk assessment. J. Agric. Food Chem. 53: 8829-8833.

Law, A.M., and Kelton, W.D. 2000. Simulation modeling and analysis. 3rd ed. Singapore: McGraw-Hill.

Li, W., Wei, C., Zhang, C., et al. 2003. A survey of arsenic species in Chinese seafood. Food Chem. Toxicol. 41(8): 1103-1110.

Lucier, G.W., and Schecter, A. 1998. Human exposure assessment and the national toxicology program. Environ. Health Perspect. 106: 623-626.

MacIntosh, D.L., Williams, P.L., Hunter, D.J., et al. 1997.Evaluation of a food frequency questionnaire foodcomposition approach for estimating dietary intake of inorganic arsenic and methylmercury. Cancer Epidemiol. Biomar. 6: 1043–1050.

Mandal, B.K., Ogra, Y., Anzai, K., and Suzuki, K.T. 2004. Speciation of arsenic in biological samples. Toxicol. Appl. Pharmacol. 198: 307–318.

Mandal, B.K., and Suzuki KT. 2002. Arsenic around the world: A review. Talanta 58: 201-235.

Meacher, D.M., Menzel, D.B., Dillencourt, M.D., et al. 2002. Estimation of multimedia inorganic arsenic intake by the US population. Hum. Ecol. Risk Assess. 8: 1697–1721.

Mead, M.N. 2005. Arsenic: in search of an antidote to a global poison. Environ. Health Perspect. 113(6): 378-388.

Mohri, T., Hisanaga, A., Ishinishi, N., 1990. Arsenic intake and excretion by Japanese adults: a 7-day duplicate diet study. Food Chem. Toxicol. 28 (7): 521–529.

Munoz, O., Devesa, V., Suner, M.A., et al. 2000. Total and inorganic arsenic in fresh and processed fish products. J. Argi. Food Chem. 48: 4369-4376.

Munoz, O., Velez, D., and Montoro, R. 1999. Optimization of the solubilization, extraction and determination of inoraganic arsenic [As (III) + As (V)] in seafood products by acid digestion, solvent extraction and hydride generation atomic absorption spectrometry. Analyst 124: 601-607.

Mushak, P., and Crocetti, A.F. 1995. Risk and revisionism in arsenic cancer risk assessment. Environ. Health Perspect. 103(7-8): 684-689.

National Cancer Institute (NCI). 2007. Hospital- based cancer registry. National Cancer Institute, Thailand.

National Research Council (NRC). 1983. Risk assessment in the federal government: Managing the process. National Research Council. Washington, DC: National Academy Press.

National Research Council (NRC). 2001. Arsenic in drinking water 2001 Update. National Research Council. Washington, DC: National Academy Press.

Nriagu, J. O. 1989. Global metal pollution. Environment. 32: 28-33.

Oberg, T., and Bergback, B. 2005. A review of probabilistic risk assessment of contaminated land. J. Soil Sed. 5: 213-224.

Office of Environmental Health Hazard Assessment (OEHHS). 2003. The Air Toxics Hot Spots Program Guidance Manual for Preparation of Health Risk Assessments. U.S. Office of Environmental Health Hazard Assessment.

Office of Natural Resources and Environmental Policy Planning (ONEP). 2004. The act of soil quality standards: arsenic. Office of Natural Resources and Environmental Policy Planning, Thailand.

Occupational Safety and Health Administration (OSHA). Inorganic arsenic[Online]. 2005. Available from http://www.osha.gov [2005, March 1].

Ohno, K., Yanasea, T., Matsuo, Y., Kimura, T., Rahman, M.H., Magara, Y., and Matsui, Y. 2007. Arsenic intake via water and food by a population living in an arsenic-affected area of Bangladesh. Sci. Total Environ. 381: 68-76.

Oshikawa, S., Geater, A., Chongsuvivatwong, V., and Chakraborti, D. 2007. Arsenic contamination of Ronphibun residents associated with uses of arsenic contaminated shallow well water other than drinking. J. Environ. Sci. Health A Tox. Hazard Subst. Environ. Eng. 42(12): 1753-1761.

Palisade. 2005. Guide to using @RISK: Risk analysis and simulation add-in for Microsoft Excel, version 4.5. NY: Palisade Press.

Patarasiriwong V., and Wongpan P. 2004. Final report of the study on the arsenic level and species in agricultural products from the Ronphibul District, Nakhon Si Thammarat Province, Thailand. Department of Environmental Promotion, Ministry of Natural Resources and Environment, Thailand.

Paustenbach, D.J. 2000. The practice of exposure assessment: a state of the art review. J. Toxicol. Environ. Health 3: 179-291.

Pollution Control Department (PCD). 1998. Investigation and analysis for operation and maintenance of arsenic contamination in Ronphibun, Thailand. Pollution Control Department, Thailand.

Pongkhamsing, N. 2003.Quantitaive analysis on soil ingestion by children between the ages of 2 and 6 years in Pathumthanee province. Master's Thesis. Department of Veterinary Public Health, Faculty of Veterinary Science. Chulalongkorn University.

Pongratz, R. 1998. Arsenic speciation in environmental samples of contaminated soil. Sci. Total Environ. 224: 133-141.

Rahman, M.A., Hasegawa, H., Rahman, M,M., and Miah, M.A.M. 2006. Influence of cooking method on arsenic retention in cooked rice related to dietary exposure. Sci. Total Environ. 370: 51–60.

Rakwong, K. 1999. Risk behaviors and sources of exposure to arsenic in schoolchildren at Tambon Ronphibun, Amphoe Ronphibun, Changwat Nakhon Si Thammarat. Master's Thesis. Department of Environmental Management, Graduate School, Prince of Songkla University.

Richardson, G.M. 1996. Deterministic versus probabilistic risk assessment: Strengths and weakness in a regulatory context. Hum. Ecol. Risk Assess. 62: 44-46.

Roberts, S.M., Weimar, W.R., Vinson, j.R., Munson, J.W., and Bergeron, R.J. 2002. Measurement of arsenic bioavailability in soil using a primate model. Toxicol. Sci. 67: 303-310.

Rodriguez, R., Ramos, J.A., and Armienta, A. 2004. Groundwater arsenic variations: The role of local geology and rainfall. Applied geochem. 19: 245-250.

Rossman, T.G. 2003. Mechanism of arsenic carcinogenesis: An integrated approach. Mutat. Res. 533: 37-65.

Roy, P., and Saha, A. 2002. Metabolism and toxicity of arsenic: A human carcinogen. Curr. Sci. 82(1): 38-45.

Ruby, M.V., Davis, A., Schoof, R., Eberle, S., and Sellstone, C.M. 1996. Estimation of lead and arsenic bioavailability using a physiologically based extraction test. Env.Sci. Tech. 30: 422-430.

Ruby, M.V., Schoof, R., Brattin, W., et al. 1999. Advances in evaluating the oral bioavilability of inorganic in soil for use in human health risk assessment. Env. Sci. Tech. 33: 3697-3705.

Saha, J.C., Dikshit, A.K., Bandyopadhyay, M.K., and Saha, K.C. 1999. A review of arsenic poisoning and its effects on human health. Critical Rev. Environ. Sci. and Tech. 29: 281-313.

Schoof, R.A., Yost, L.J., Eickhoff, J., Crecelius, E.A., Cragin, D.W., and Meacher, D.M. 1999. A market basket survey of inorganic arsenic in food. Food Chem. Toxicol. 37: 839–846.

Shannon, R.L., and Strayer, D.S. 1989. Arsenic-induced skin toxicity. Hum. Toxicol. 8: 99-104.

Sheppard, S.C.1995. Parameters values to model the soil ingestion pathway. Environ Monit. Assess. 34: 27–44.

Simon, S.L. 1998. Soil ingestion by humans: a review of history, data, and etiology with application to risk assessment of radioactively contaminated soil. Health Phys. 74(6): 647-72.

Siripitayakunkit, U. 2000. Survey of chronic poisoning in Ronphibun, Nakron Si Thammarat, Thailand. The proceeding of 6th International Conference on the Biochemistry of Trace Elements, Guelph, Canada.

Slob, W., and Pieters, M.N. 1998. A probabilistic approach for deriving acceptable human intake limits and human health risks from toxicological studies: General framework. Risk Anal. 18: 787–798

Slayton, T.M., Beck, B.D., Reynolds, K.A., et al. 1996. Issues in arsenic cancer risk assessment. Environ. Health Perspect. 104 (10): 1012-1018.

Smedley, P.L., and Kinniburgh, D.G. 2002. A review of the source, behaviour and distribution of arsenic in natural waters. Applied geochem. 17: 517-568.

Smith, A.H., Hopenhayn-Rich, C., Bates, M.N., et al. 1992. Cancer risks from arsenic in drinking water. Environ. Health Perspect. 97: 259-267.

Smith, M. 2002. Food safety in Europe: Risk assessment of chemicals in food and diet, overall introduction. Food Chem. Toxical. 40: 141-144.

Smith, N.M., Lee, R., Heitkemper, D.T., Cafferky, K.D., Haque, A., and Henderson, A.K. 2006. Inorganic arsenic in cooked rice and vegetables from Bangladeshi households. Sci. Total Environ. 370: 294–301.

Smith, R.L. 1994. Use of Monte Carlo simulation for human exposure assessment at a Superfund site. Risk Anal. 14(4): 433-439.

South-East Asia Regional Office (SEARO). 2001. Arsenic contamination in groundwater affecting some countries in the South-East Asia region. Regional Office of Southeast Asia, World Health Organization.

Stanek, E.J., and Calabrese, E.J. 1991. A guide to interpreting soil ingestion studies: I. Development of a model to estimate the soil ingestion detection level of soil ingestion studies. Regul. Toxicol. Pharmacol. 13: 263–277.

Stanek, E.J., and Calabrese, E.J. 1995a. Daily estimates of soil ingestion in children. Environ. Health Perspect. 103(3): 276-285.

Stanek, E.J., and Calabrese, E.J. 1995b. Soil ingestion estimates for use in site evaluations based on the best tracer method. Human Eco. Risk Assess. 1(2): 133-156.

Stanek, E.J., Calabrese, E.J., and Barnes, R. 1999. Soil ongestion estimates for children in Anconda using tracer elements concentrations in different particle size fractions. Hum. Eco. Risk Assess. 5: 547-558.

Stanek, E.J., Calabrese, E.J., and Stanek, E.J. 2000. Daily soil ingestion estimates for children at a Superfund site. Risk Anal. 20(5): 627-35.

Stanek, E.J., Calabrese, E.J., and Zorn, M. 2001. Soil ingestions distribution for monte carlo risk assessment in children. Human Eco. Risk Assess. 7(2): 357-368.

Stanek, E.J., Calabrese, E.J., Barnes, R., and Pekow, P. 1997. Soil ingestion in adults-Results of a second pilot study. Ecotoxicol. Environ. Saf. 36(3): 249-257.

Sternowsky, H.J., Moser, B., and Szadkowsky, D. 2002. Arsenic in breast milk during the first 3 months of lactation. Int. J. Hyg. Environ. Health 205(5): 405-409.

Suwanmanee, A. 1990. Distribution of arsenic in the environment of Amphoe Ronphibun, Changwat Nakhon Si Thammarat. Master's Thesis. Department of Environmental Management, Graduate School, Prince of Songkla University.

Tao, S.S., and Bolger, P.M. 1999. Dietary arsenic intake in the United States: FDA total diet study, September 1991-December 1996. Food Addit. Contam. 16: 465-472.

Thailand, Food and Drug Administration (ThaiFDA). 2003. Standard of arsenic in food. Food and Drug Administration, Thailand.

Thermphonboon, W. 2003. Influence of occupations on the incidence of soil ingestion in Thai people 30-50 years of age in Patthalung province. Master's Thesis. Department of Veterinary Public Health, Faculty of Veterinary Science, Chulalongkorn University.

Thompson, K.M., Burmaster, D.E., and Crouch, E.A.C. 1992. Monte Carlo techniques for quantitative uncertainty analysis in public health assessments. Risk Anal. 12: 53-63.

Tongboriboon, T. 1997. Arsenic contamination in aquatic organism from Tambon Ronphibun to Pak Phanang river basin, Changwat Nakron Si Thammarat. Master's Thesis. Department of Environmental Management, Graduate School, Prince of Songkla University.

Tseng, W.P. 1977. Effects and dose-response relationships of skin cancer and blackfoot disease with arsenic. Environ. Health Perspect. 19: 109-119.

Tseng, W.P., Chu, H.M., How, S.W., Fong, J.M., Lin, C.S., and Yeh, S. 1968. Prevalence of skin cancer in an endemic area of chronic arsenium in Taiwan. J. Natl. Cancer Inst. 40: 453-463.

Tsuda, T., Inoue, T., Kojima, M., and Shigeru, A. 1995. Market basket and duplicate portion estimation of dietary intakes of cadmium, mercury, arsenic, copper, manganese, and zinc by Japanese adults. J. AOAC Inter. 78: 1363-1368.

Uchino, T., Roychoedhury, T., Ando, M., and Tokunaga, H. 2006. Intake of arsenic from water, food composites and excretion through urine, hair from a studied population in West Bengal, India. Food Chem. Toxicol. 44: 455-461.

United Kingdom Ministry of Agriculture, Fisheries and Food (UKMAFF). 1997. Lead, arsenic and other metals in food. Food Surveillance Paper No 52. Ministry of Agriculture, Fisheries and Food, London, UK.

United States Environmental Protection Agency (U.S.EPA). 1984. Health Assessment Document for Arsenic. United States Environmental Protection Agency. EPA 600/8-32-021F.

United States Environmental Protection Agency (U.S.EPA). 1987. The risk assessment guidelines of 1986. United Staets Environmental Protection Agency. EPA/600/8-87/045.

United States Environmental Protection Agency (U.S.EPA). 1988. Special report on ingested inorganic arsenic, skin cancer nutritional essentiality. United States Environmental Protection Agency. EPA/625/3-87/013.

United States Environmental Protection Agency (U.S.EPA). 1989. Risk assessment guidance for Superfund: Volume I. Human health evaluation manual (part A, baseline risk assessment). United States Environmental Protection Agency. EPA /540/1-89/002.

United States Environmental Protection Agency (U.S.EPA). 1992. Final guidelines for exposure assessment. United States Environmental Protection Agency.

United States Environmental Protection Agency (U.S.EPA). 1994. Use of Monte Carlo simulation in risk assessments. Region 3, Philadelphia. United States Environmental Protection Agency. EPA/903/F-94/001.

United States Environmental Protection Agency (U.S.EPA). 1995. Use of Monte Carlo simulation in performing risk assessment (Technical section). Region 8, Denver. United States Environmental Protection Agency.

United States Environmental Protection Agency (U.S.EPA). 1997a. Exposure Factors Handbook. United States Environmental Protection Agency. EPA/600/P-95/002Fa.

United States Environmental Protection Agency (U.S.EPA). 1997b. Relative bioavailability of arsenic in mining wastes. Region 8, Denver, United States Environmental Protection Agency.

United States Environmental Protection Agency (U.S.EPA). 1997c. Policy for use of probabilistic analysis in risk assessment. United States Environmental Protection Agency.

United States Environmental Protection Agency (U.S.EPA). 1997d. Guiding principles for Monte Carlo analysis. United States Environmental Protection Agency. EPA/630/R-97/001.

United States Environmental Protection Agency (U.S.EPA). 2000a. Superfund probabilistic risk assessment to characterize uncertainty and variability. United States Environmental Protection Agency.

United States Environmental Protection Agency (U.S.EPA). 2000b. Risk characterization handbook. United States Environmental Protection Agency. EPA/100/B/00-002.

United States Environmental Protection Agency (U.S.EPA). 2000c. Data quality objectives process for hazardous waste site investigations. United States Environmental Protection Agency. EPA/600/R-00/007.

United States Environmental Protection Agency (U.S.EPA). 2001a. Risk Assessment Guidance for Superfund: Volume III-Part A, Process for Conducting Probabilistic Risk Assessment. United States Environmental Protection Agency. EPA/540/R-02/002.

United States Environmental Protection Agency (U.S.EPA). 2001b. Draft guidance on calculation of upper confidence limits for exposure point concentrations at Superfund site. United States Environmental Protection Agency.

United States Environmental Protection Agency (U.S.EPA). 2002. A review of the reference dose and reference concentration process. United States Environmental Protection Agency. EPA/630/P-02/002F.

United States Environmental Protection Agency (U.S.EPA). 2005. Estimation of relative bioavailability of arsenic in soil and soil-like materials by in vivo and in vitro methods. Region 8, Denver, United States Environmental Protection Agency.

United States Food and Drug Administration (U.S.FDA). 1997. Total arsenic data from an electronic database consisting of all results from total diet study market baskets collected from 1986 to 1994. United States Food and Drug Administration.

Urieta, I., Jalon, M., and Eguilero, I. 1996. Food surveillance in the Basque Country (Spain). II. Estimation of the dietary intake of organochlorine pesticides, heavy metals, arsenic, aflatoxin M1, iron and zinc through the total diet study, 1990/91. Food Addit. Contam. 13: 29-52.

Vahter, M. 2002. Mechanisms of arsenic biotransformation. Toxicology 181: 211-217.

Valentine, J.L., Kang, H.K., and Spivey, G. 1979. Arsenic levels in human blood, urine and hair in response to exposure via drinking water. Environ. Res. 20: 24-32.

Van-Wijnen, J.H., Clausing, P., and Brunekreef, B. 1990. Estimated soil ingestion by children. Environ. Res. 51: 147-162.

Visoottiviseth, P., Francesconi, K., and Sridokchan, W. 2002. The potential of Thai indigenous plant spcies for the phytoremediation of arsenic contaminated land. Environ. Pollut. 118: 453-461.

Vitayavirasak, B. 1999. The report of arsenic contamination in drinking water and its carcinogenic risk upon population of villages in Tambon Ronphibun, Amphoe Ronphibun, Changwat Nakhon Si Thammarat. Research and Development Office, Prince of Songkla University.

Vitayavirasak, B., Rakwong, K., and Chatchawej, W. 2005. Environmental arsenic exposure of schoolchildren in a former tin mining and smelting community of southern Thailand. Environ. Sci. 12(4): 195-205.

Vose, D. 2000. Risk analysis: A quantitative guide. 2nd ed. England: John Wiley and Sons Press.

Watanabe, C., Kawata, A., Sudo, N., Sekiyama, M., Inaoka, T., Bae, M., and Ohtsukaa, R. 2004. Water intake in an Asian population living in arsenic-contaminated area. Toxicol. Appl. Pharmacol. 198: 272– 282.

Wattansen, K. 2000. A geophysical study of an arsenic contaminated area in the Ronphibun district, southern Thailand. Doctoral dissertation. Department of Geochemistry, Graduate School, University of Uppsala, Sweden.

Wester, R.C., Maibach, H.I., Sedik, L., Melendres, J., and Wader, M. 1993. In vivo and in vitro percutaneous absorption and skin decontamination of arsenic from water and soil. Fund. Applied Toxicol. 20: 336-340.

World Health Organization (WHO). 1985. Guidelines for the study of dietary intakes of chemical contaminants. World Health Organization, Geneva.

World Health Organization (WHO). 2001. Environmental Health Criteria 224: Arsenic and Arsenic Compounds. World Health Organization, Geneva.

Williams, P.R.D., and Paustenbach, D.J. 2002. Risk characterization: principles and practice. J. Toxicol. Environ. Health 5: 337-406.

Williams, T.M., Fordyce, A., Paijitprapapor, A., and Charoenchaisri, P. 1996. Arsenic contamination in the surface drainage and groundwater in part of the Southeast Asian tin belt, Nakhon Si Thammarat province, Southern Thailand. Environ. Geo. 27: 16-33.

Williams, T.M., Rawlins, B.G., Smith, B., and Breward, N. 1998. In vitro determination of arsenic bioavailability in contaminated soil and mineral beneficiation waste from Ronphibun, Southern Thailand: a basic for improved human health risk assessment. Environ. Geochem. Health 20: 169-177.

Wongsanoon, J., Booncharoemkit, S., Wongpan, P., and Chaiyo, L. 2000. Study on arsenic contamination in dust and rainwater at Ronphibun district Nakhon sritammaraj province. Environmental Research and Training Center, Department of Environmental Quality Promotion, Thailand.

Yost, L.J., Schoof, R.A., and Aucoin, R. 1998. Intake of inorganic arsenic in the North American diet. Human Ecol. Risk Assess. 4: 137-152.

Zartarian, V.G., Xue, J., Ozkaynak, H, et al. 2006. A probabilistic arsenic exposure assessment for children who contact CCA-treated playsets and decks, Part 1: Model methodology, variability results, and model evaluation. Risk Anal. 26(2): 515-531.

Zheng, Y., Wu, J., and Ng, J.C. 2002. The absorption and excretion of fluoride and arsenic in humans. Toxicol. Lett. 133(1): 77-82.

APPENDIX

Monte Carlo method

Monte Carlo simulation is defined as a scheme employing random numbers that is Uniform (0,1) random variable which is used for solving certain stochastic or deterministic problems. Usually a definite integral of a function is evaluated by using the fundamental theorem of calculus. However, when there is no close form for the integral this method would be rather difficult. In this case, Monte Carlo method can be used to approximate the integral. The method is also apparent in the evaluation of multidimensional integral. To suppose that we would like to evaluate the integral

$$I = \int_a^b g(x)dx$$

where *g(x)* is a real valued function that is not analytical integral. In practical Monte Carlo simulation would probably not be used to evaluate a single integral, since there are more efficient numerical analysis techniques for this purpose. It is more likely to be used on multiple integral problems. Let *Y* is the random variable *(b-a)g(X)*, where *X* is a continuous random variable distributed uniformly on *U(a,b)*, then the expected value of *Y* is

$$E(Y) = E[(b-a)g(X)]$$

$$= (b-a)E[g(X)]$$

$$= (b-a)\int_a^b g(x)fx(x)dx$$

$$= (b-a)\frac{\int_a^b g(x)dx}{b-a}$$

$$= I$$

where $fx(x) = 1/(b-a)$ is the probability density function of a $U(a,b)$ random variable. Thus, the problem of evaluating the integral has been reduced to one of estimating the expected value $E(Y)$. In particular, the estimatation of $E(Y)$ equals to I by the sample mean:

$$\boldsymbol{Y}(\mathrm{n}) = \frac{\sum_{i=1}^{n} Yi}{n} = (b-a)\frac{\sum_{i=1}^{n} g(Xi)}{n}$$

where $X_1, X_2, \ldots, Xn$ are $U(a,b)$ random variables. Furthermore, it can be shown that $E[\boldsymbol{Y}(n)]$, that is $\boldsymbol{Y}(n)$ is an unbiased estimator of I and $Var\ [\boldsymbol{Y}(n)] = Var\ (Y) / n$. Assuming that $Var(Y)$ is finite, it follows that $\boldsymbol{Y}(n)$ will be arbitrarily close to I for sufficient large n with probability 1.

The basic Monte Carlo method for computing I numerically is given as follows draw observations $(x)^{(l)}$ from the density $f(x)$, $l = 1, ,,\ldots,$ L and approximate I. The Monte Carlo method for integration is an application of the strong law of large numbers where U is uniform distribution over (0,1):

$$\mathbf{E}\,[(\mathrm{f}(\mathrm{U})] = \int_{0}^{1} \mathrm{f}(x)dx$$

Figure A.1 shows conceptual model of Mote Carlo analysis, a random sample of each parameter V is selected by sampling randomly on the interval (0,1) a value of the parameter K. The selected value of k is transformed into the value, v, of parameter V by choosing the smallest value of v such that the probability that value, v, exceeds the actual value of the parameter V is less than or equal to k ,e.g., $P(v>V) \leq t$. If n values of V are needed, this procedure is repeated n times and each time the procedure is repeated every value from the range (0, 1) has an equal chance of being selected.

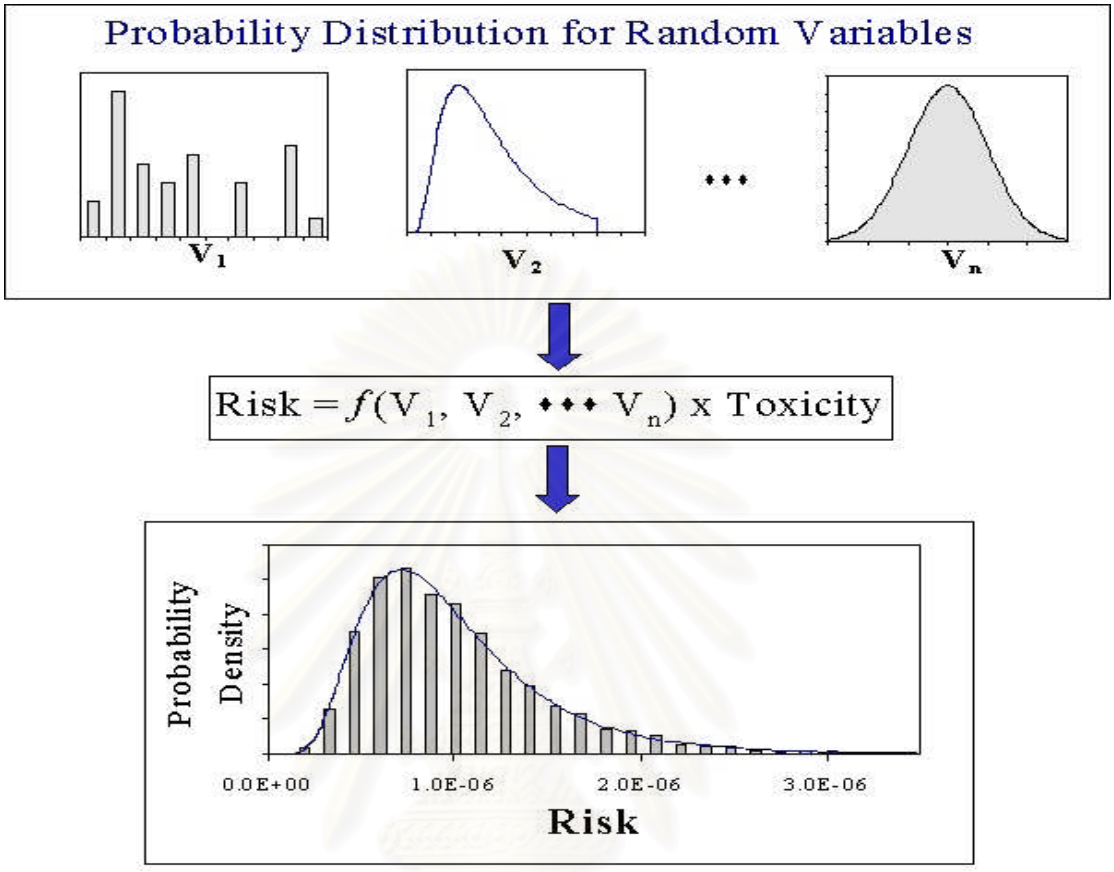


Figure A.1 Monte Carlo analysis. V_1, V_2,...Vn refer to exposure factors such as concentration of arsenic, ingestion rate, and exposure time that are characterized by probability distributions. Risk estimate is calculated for each set of random values. Repeatedly sampling (Vi) results in a frequency distribution of risk, which can be described by a PDF. Source: U.S.EPA, (2001a).

Algorithm;

Step 1: Set $K = 0$

Step 2: Input N as iteration

Step 3: Generate a random number U

Step 4: $K = K + f(U)$

Step 5: Go to step 3 until the *Nth* random number is generated

Step 6: Return the approximation of the integral of f as K/N

Monte Carlo simulation is run repeated by using difference values for each of the uncertainty input parameters each time. The values of each input variables are generated based on the probability distribution. Monte Carlo method requires the generation of uniformly distributed random numbers between 0 and 1. There are a variety of methods for generating pseudo-random numbers. The most random generators are based upon the linear congruential generator. Uniformly distributed random numbers are used as the input to algorithms that generate random numbers from other types of distributions. These methods include the inverse transform, composition, the method of convolution, and the acceptance-rejection method and in addition methods exist for simulation of jointly distributed random variables. To implement a mixture distribution in a Monte Carlo simulation requires some careful programming (Cullen and Frey, 1999; Frey and Rhodes, 1998)

Probability distribution

In a graphical representation of a probability distribution function ,PDF, (Figure A.2), the y-axis indicate the probability density or relative frequency and the x-axis represent a continuous scale for a measured variable. The total area under the PDF curve represents all the items in the original data. Thus, if an arbitrary vertical strip under PDF curve is selected, the probability that the variable will have a value which lies between the lower and upper bounds of the given strip is equal to the ratio of the area of the vertical strip to the total area under the curve.

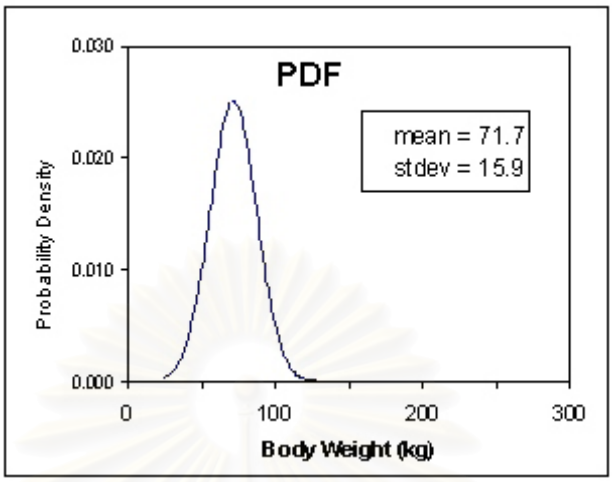


Figure A.2 PDF curve (U.S.EPA, 2001a)

A probability distribution can also be represented by a cumulative distribution function (CDF), F(x). The CDF (Figure A.3) is obtained by adding the individual increments of the PDF. The CDF is defined as the probability that any outcome in X is less than or equal to stated limiting value x. Mathematical is follow:

$$F(x) = \text{Prob}[X \leq x] \int_{-\infty}^{x} fx(x)dx$$

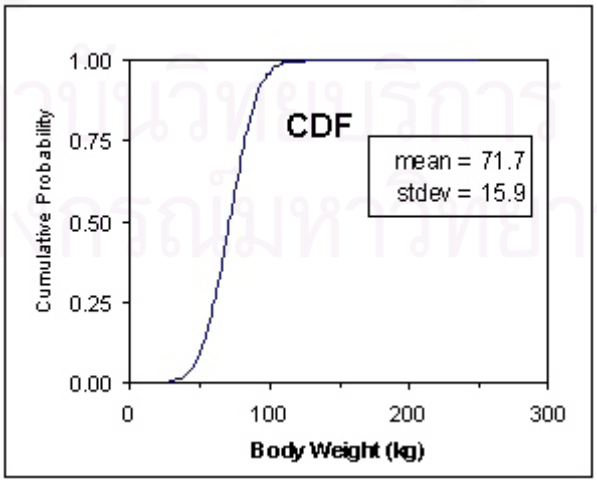


Figure A.3 CDF curve (U.S.EPA, 2001a)

To assign a value to a given variable described by a particular distribution and its parameter, a random number from that distribution and bounded by those parameters, has to be generated. The normal procedure followed to accomplish this is to utilize the inverse of the CDF. Some form of distribution used in this study described below:

Uniform distribution

There are two parameters of uniform distribution of minimum (a) and maximum (b). They indicate the range of values for the random variate X. Variable x can be calculated knowing the PDF and CDF.

$$PDF: \quad f(x) = \frac{1}{b-a} \qquad a \leq x \leq b$$

$$CDF: \quad F(x) = \int_a^x f(x)dx = \int_a^x \frac{dx}{b-a} = \frac{x-a}{b-a} \qquad a \leq x \leq b$$

Triangular distribution

There are three parameters of the triangular distribution are minimum (a), maximum (b), and the shape parameter or most likely (c) values. The PDF for triangular distribution is:

$$PDF: \quad f(x) = \frac{2(x-a)}{(b-a)(c-a)} \qquad a \leq x \leq c$$

$$PDF: \quad f(x) = \frac{2(x-a)}{(b-a)(c-a)} \qquad c \leq x \leq b$$

The CDF for triangular distribution is given by:

$$CDF: \quad F(x) = \int_a^x f(x)dx = \int_a^x \frac{2(x-a)}{(b-a)(c-a)}dx \qquad a \leq x \leq c$$

$$CDF: \quad F(x) = \int_a^x f(x)dx = \int_a^x \frac{2(x-a)}{(b-a)(c-a)}dx \qquad c \leq x \leq b$$

Normal distribution

The parameters for normal distribution are the mean (μ) and standard deviation (σ). They determine the location of the random variable and the shape of distribution curve, respectively. The PDF of normal distribution is:

$$\textbf{PDF:} \quad f(x) = \frac{1}{\sqrt{2\pi\sigma^2}}\exp\left(-\frac{(x-\mu)^2}{2\sigma^2}\right) dx \qquad -\infty < x < \infty$$

The CDF for the normal distribution can be estimated as follows:

$$CDF: \quad F(x) = \int_{-\infty}^{x} \frac{1}{\sqrt{2\pi\sigma^2}}\exp\left(-\frac{(x-\mu)^2}{2\sigma^2}\right) dx \qquad -\infty < x < \infty$$

Lognormal distribution

Similar to the normal distribution, the parameters for lognormal distribution are the mean (μ) and standard deviation (σ) but the mean and standard deviation are estimated from the geometric mean and geometric standard deviation or log transformation of a sample. The PDF of lognormal distribution is:

$$\textbf{PDF:} \quad f(x) = \frac{1}{x\sigma\sqrt{2\pi\sigma}}\exp\left(-\frac{(\ln x-\mu)^2}{2\sigma^2}\right) dx \qquad 0 < x < \infty$$

The CDF for lognormal distribution can be estimated as follows:

$$\text{CDF:} \qquad F(x) = \int_0^{\infty} \frac{1}{x\sigma\sqrt{2\pi\sigma}} \exp\left(-\frac{(\ln x - \mu)^2}{2\sigma^2}\right) dx \qquad 0 < x < \infty$$

Extvalue distribution

This distribution is sometimes also called the Fisher-Tippett distribution or log-Weibull distribution and it is the distribution of the extreme order or the maximum for a distribution. It has a location parameter α and scale parameter β. The PDF and CDF of Extvalue distribution are:

$$PDF: \qquad f(x) = \left(\frac{1}{\beta}\right) \exp\left(-\frac{x-\alpha}{\beta}\right) exp\left[-exp\left(-\frac{x-\alpha}{\beta}\right)\right]$$

$$CDF: \qquad F(x) - exp\left[-exp\left(-\frac{x-\alpha}{\beta}\right)\right] \qquad \beta > 0, -\infty < x < \infty$$

Parameter estimation of probability distribution

Based upon visual inspection of an empirical distribution of data and consideration of processes that generated the data, the analyst can make a judgment regarding selection of one or more candidate parametric distributions to fit to the data set. The method of Maximum likelihood estimation (MLE) is the most typical techniques used for estimating the continuous parameter.

Maximum Likelihood Estimation (MLE)

The MLE method involves the selection of parameter values that characterize a distribution which was most likely to yield the observed data set. A likelihood function for independent samples is defined as the product of the PDF evaluated at

each of the sample values. For a continuous random variable, the likelihood function is:

$$L(\theta 1, \theta 2, \ldots \theta k) = \prod_{i=1}^{n} f(xi \mid \theta 1, \theta 2, \ldots \theta k)$$

where:

θ1, θ2, …, θk = parameters of the parametric probability distribution model.

K = number of parameters for the parametric probability distribution model.

xi = values of the random variable, for i = 1, 2, …, n

n = number of data points in the data set.

f = probability density function.

The general idea behind MLE is to choose values of the parameters of the fitted distribution so that the likelihood that the observed data is a sample from the fitted distribution is maximized. The likelihood is calculated by evaluating the probability density function for each observed data point and multiplying the results. The parameter values may be changed to change the value of the likelihood function until a maximum is reached.

Goodness of fit to probability distribution model

There are many goodness-of-fit tests available from which to evaluate the goodness of fit of an assumed distribution model with respect to the data. Two general types of approaches for evaluating goodness of fit include probability plots and statistic tests. Probability plots are widely recognized to be a subjective method for determining whether or not data contradict an assumed model based upon visual inspection (Cullen and Frey, 1999). A graphical technique uses in @RISK is to compare the fitted distribution with the original data set plotted.

Three goodness-of-fit tests for parametric distributions are the Chi-square test, the Kolmogorov-Smirnov (K-S) test, and the Anderson-Darling (A-D) test in @RISK software. The advantage of Chi-square test is its flexibility, it can be used to test any distribution. However, a disadvantage of this method is that it has lower power than other statistical tests (Cullen and Frey, 1999). K-S test is based on evaluation of the maximum difference in the cumulative probability of the fitted distribution versus that of a data point. An attractive feature of K-S test is that it is a distribution-free test of goodness of fit. K-S test tends to be more sensitive to deviations of a good fit near the center of the distribution compared to at the tails.

The A-D test is based on a weighted square of the vertical distance between the empirical and fitted distributions. The A-D test gives more weight to the tails than does the K-S test and therefore is more sensitive to deviations in the fit at the tails of a distribution (Cullen and Frey, 1999). Thus, in the present study uses A-D test for probability model. The A-D test statistic is defined as:

$$A_n^2 = n \int_{-\infty}^{+\infty} |F_n(x) - \mathcal{F}(x)|^2 \; \Psi(x) f(x) dx$$

where: the weight function $\psi(x) = 1 / \{ \mathcal{F}(x) [1 - \mathcal{F}(x)]\}$. Thus A^2_n is just the weight average of the squared differences $[F_n(x) - \mathcal{F}(x)]^2$ and the weights are the largest for $\mathcal{F}(x)$ close to 1 (right tail) and $\mathcal{F}(x)$ close to 0 (left tail). If we let $Zi = \mathcal{F}(X_{(i)})$ for $i = 1, 2, \ldots, n$, then it can be shown that

$$A_n^2 = (\left\{\sum_{i=1}^{n} (2i-1)[\ln Zi + \ln(1 - Zn + 1 - i)]\right\}/n) - n$$

which is the form of the statistic used for actual computation. Since A^2_n is a weight distance, the form of test is to reject the null hypothesis H_0 of A^2_n exceeds some critical vale $a_{n,\,1-\alpha}$, where α is the level of test.

It noted that, @RISK program is not sufficiently documented with regard to the definition of the PDF or of the parameter estimation algorithms employed for a

particular distribution. In the absence of knowledge of the actual definitions used in @RISK, it is quite likely that differences in parameter estimate methods that literature reviews above because may be of different definition. Thus, without knowledge of the specific parameter estimation used in @Risk, it is possible that any differences compared to other programs could be because of different parameter estimation methods.

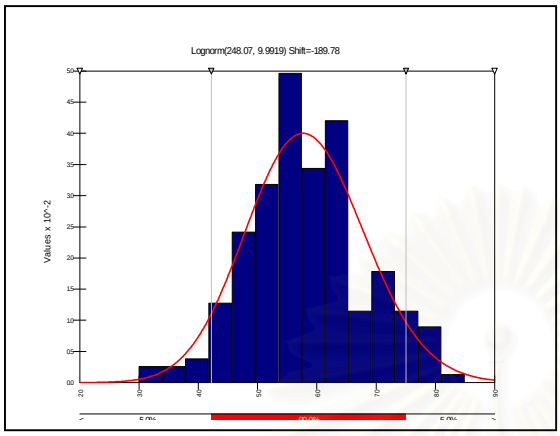
@RISK simulation

The random variables are assigned a probability distribution using the best fit feature available in @Risk. Best fit is a built in feature of @Risk that attempts to fit the best probability distribution that underlines the data in hand. Best fit tries to find the set of distributional parameters that make the closest match between a distribution function and the data sets and ranks the ten best matches for the modeler to choose from them. After the fit is run, @Risk does not produce an absolute answer but rather identifies a distribution that most likely produced the data being analyzed.

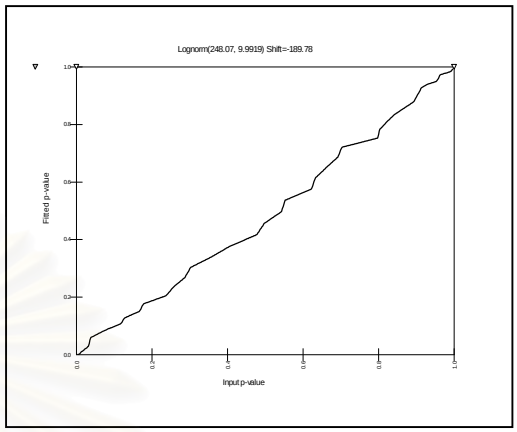
When best fit is run @Risk returns a graphical representation of the fit and a statistical chart with the major distributional statistics. The graphical are representation the major distributional statistics for each of the fitted variable. The graphs presents below, called comparison graphs, Probability-Probability (P-P), Quantile-Quantile (Q-Q), and difference graphs represent the distribution for the input data against the fitted distribution. The comparison graph superimposes the fitted data and the fitted distribution on the same graph, allowing the modeler to visually compare them either as density or cumulative curves. The P-P graph plots the distribution of the input data P(i) versus the distribution of the result (F(xi)). If the fit is a good fit the plot will be nearly linear. The Q-Q graph plots the percentile values of the input distribution (xi) versus percentile values of the result (F-1(Pi)). A difference graph displays the absolute error between the fitted distribution and the input data. A perfect fit would have an absolute error of zero throughout the variable range. These graphs allow the modeler to determine if the fitted distribution matches

the input data in specific areas. Evaluating the fit with a comparison graph becomes imperative when one wants to have a good match in these specific areas.

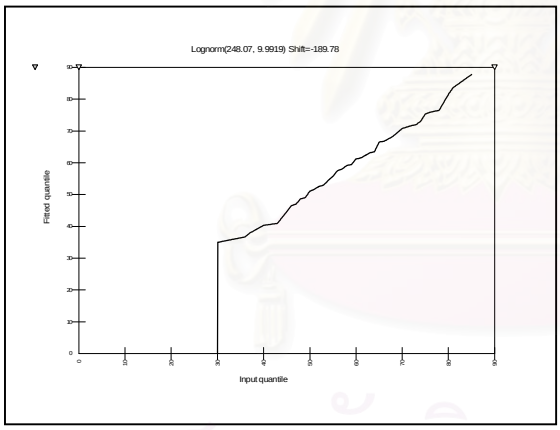
Figure A.4 to A.12 shows the graphical distribution of exposure variables. The 90% confidence interval is presented at the bottom of the graph. Left and right X are just the boundaries of the 90% confidence interval (for the fitted distribution). Left and Right P are the probabilities associated with the 90% confidence interval, left P is 5% and Right P is 95% always for the fit distribution. If the fit is a perfect fit, then all of the statistics for the fitted and input distributions will correspond.



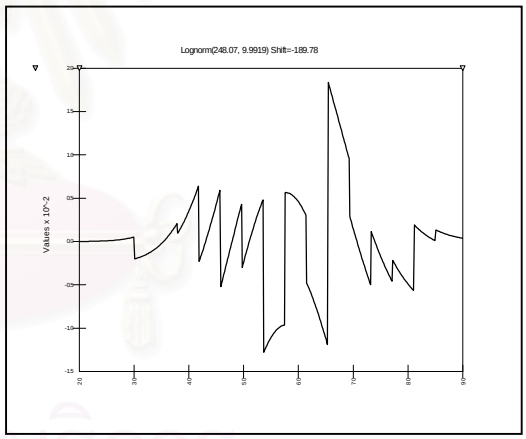
Comparison



P-P plot

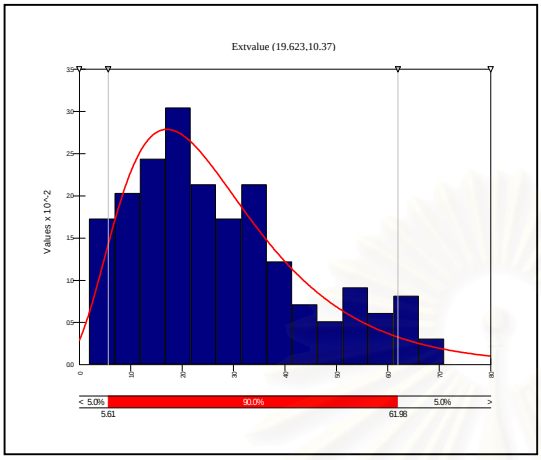


Q-Q plot

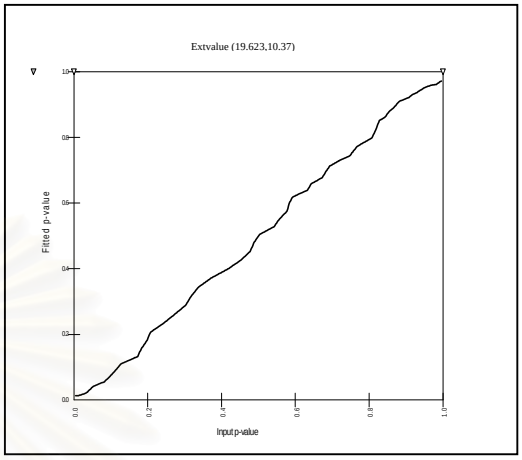


Difference

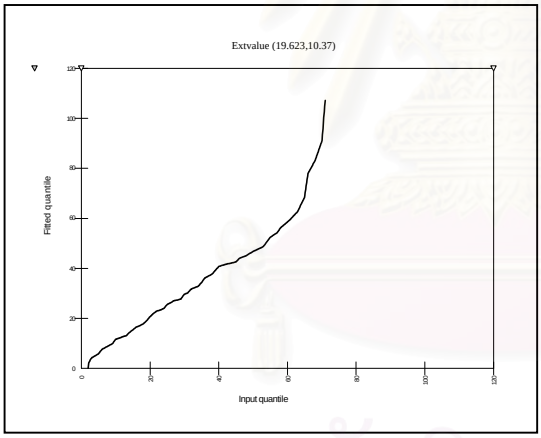
Figure A.4 Graphical distribution for adults body weight



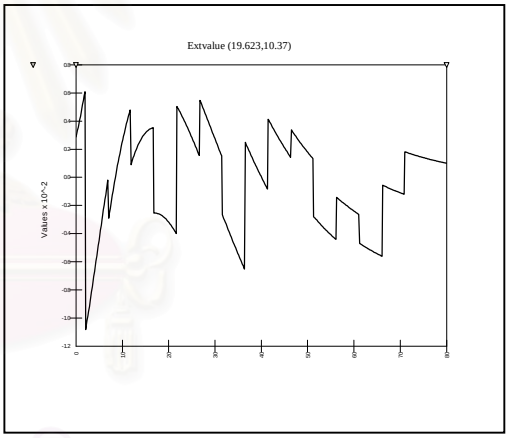
Comparison



P-P plot

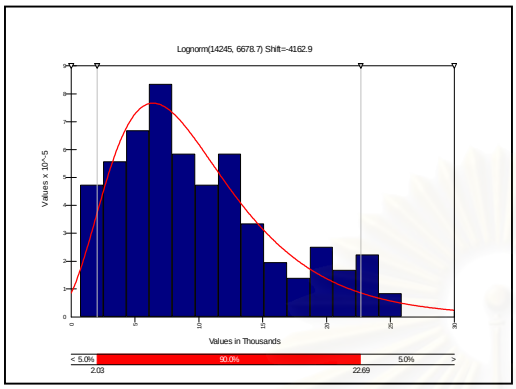


Q-Q plot

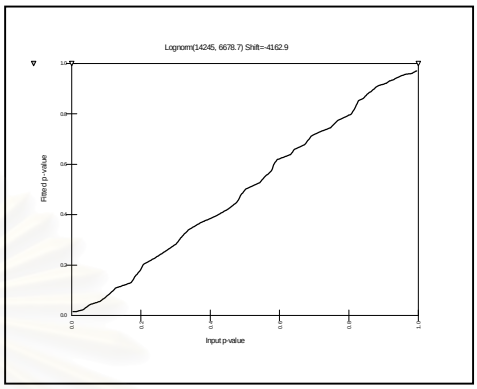


Difference

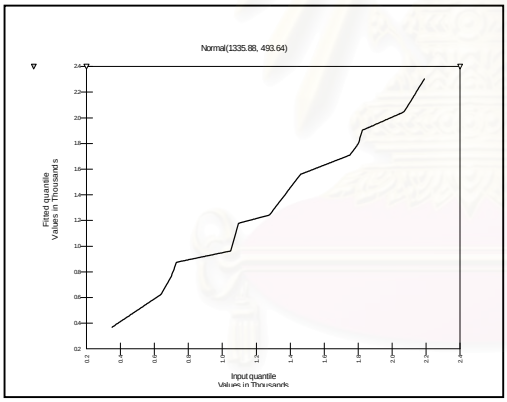
Figure A.5 Graphical distribution for exposure duration in adults



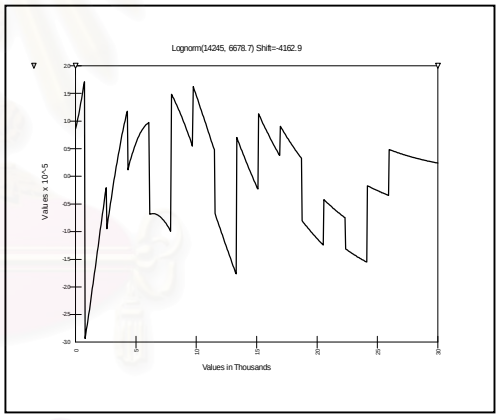
Comparison



P-P plot

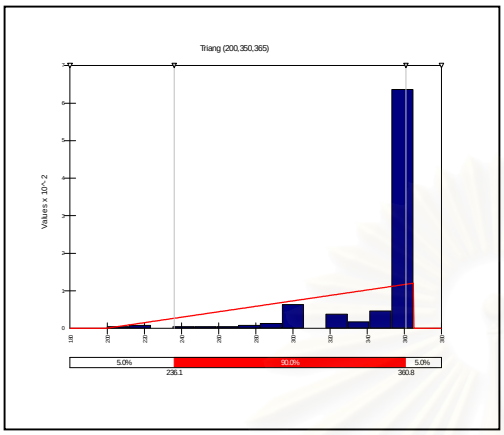


Q-Q plot

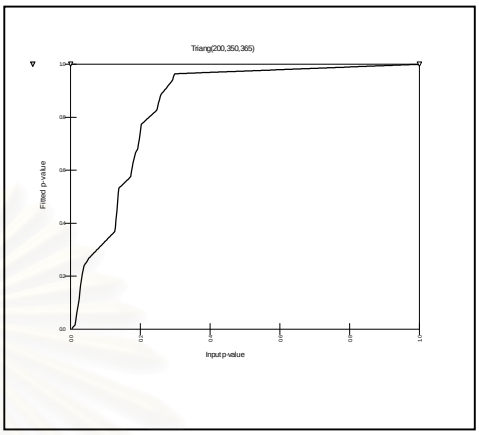


Difference

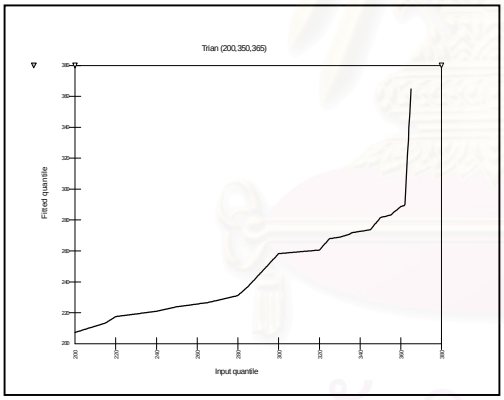
Figure A.6 Graphical distribution for averaging time for noncancer effects in adults



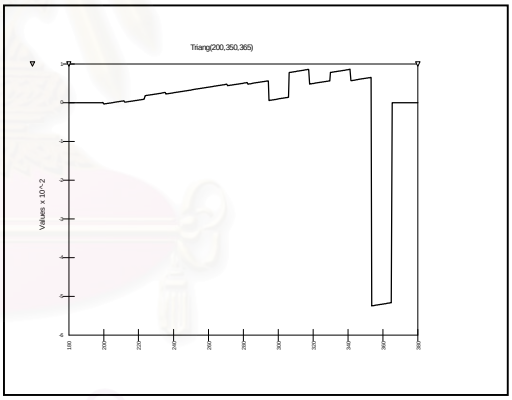
Comparison



P-P plot

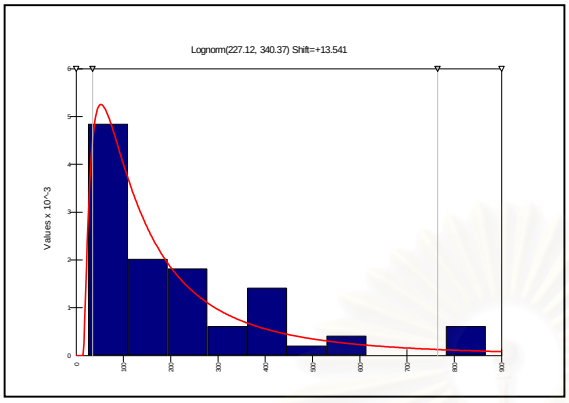


Q-Q plot

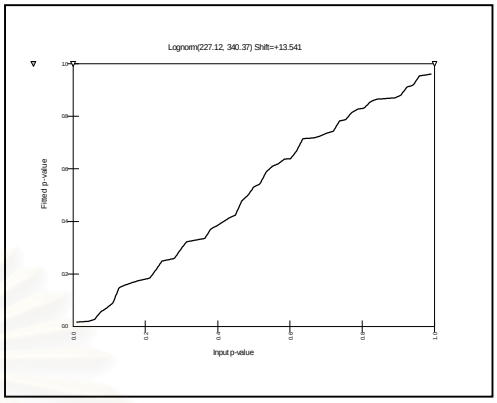


Difference

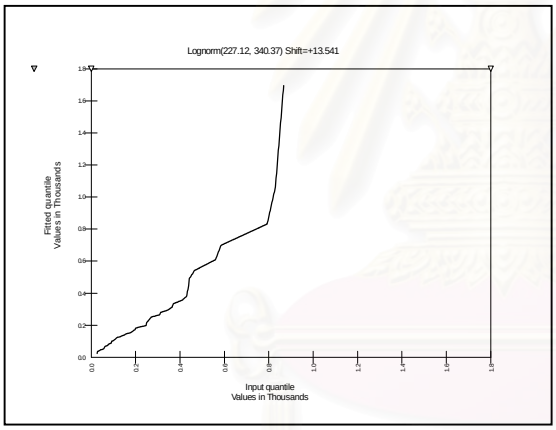
Figure A.7 Graphical distribution for exposure frequency in both children and adults



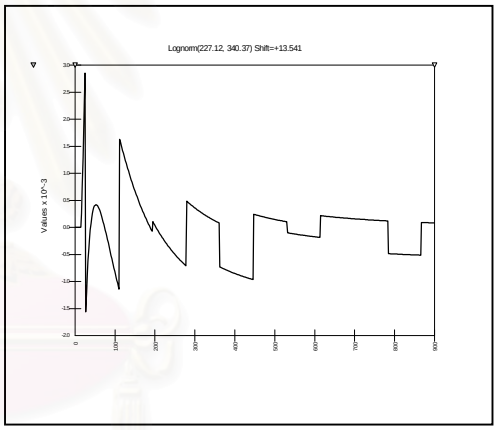
Comparison



P-P plot

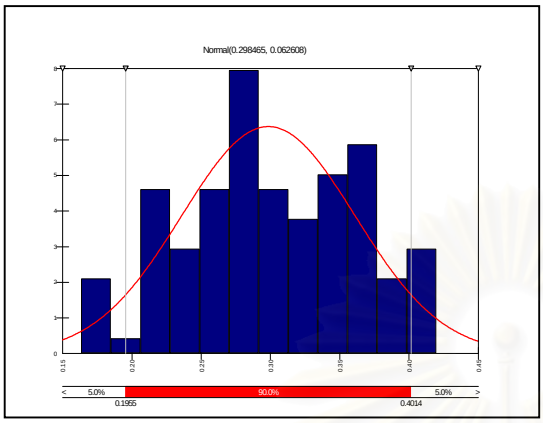


Q-Q plot

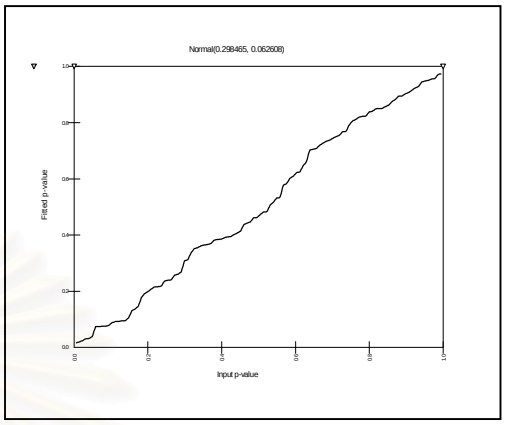


Difference

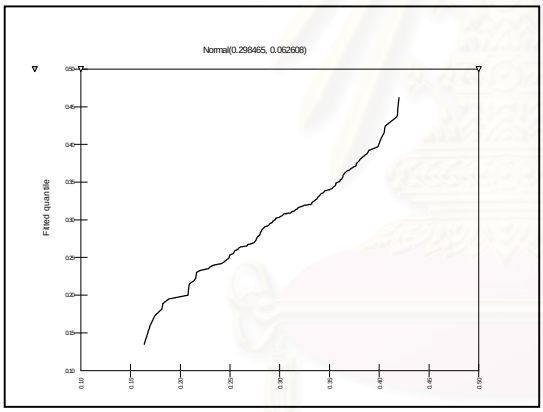
Figure A.8 Graphical distribution for arsenic concentration in soil



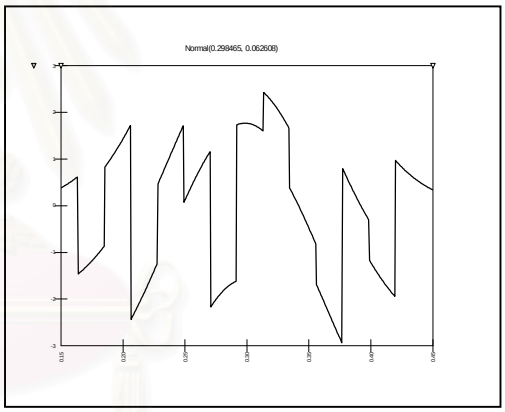
Comparison



P-P plot

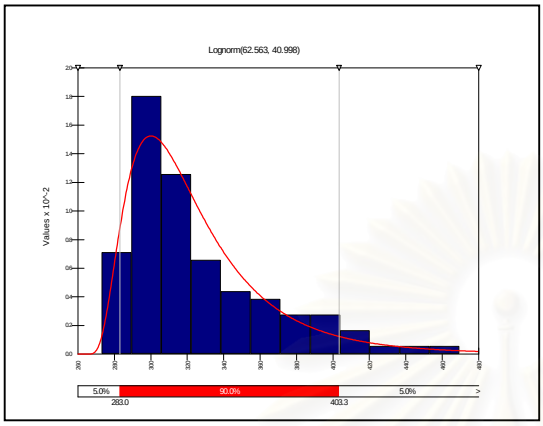


Q-Q plot

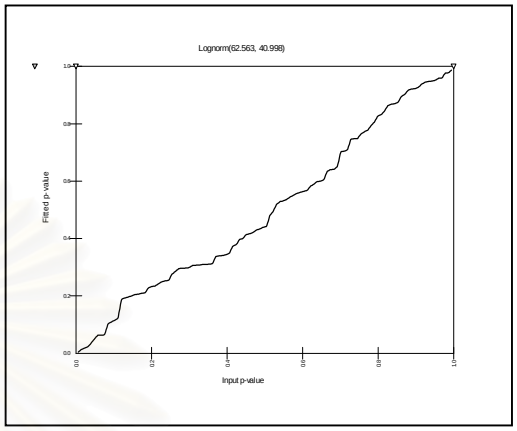


Difference

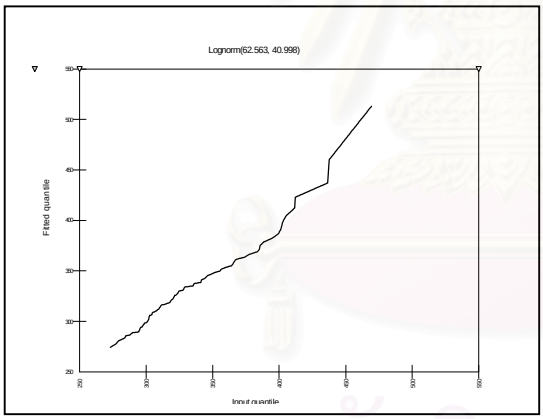
Figure A.9 Graphical distribution for arsenic concentration in meal



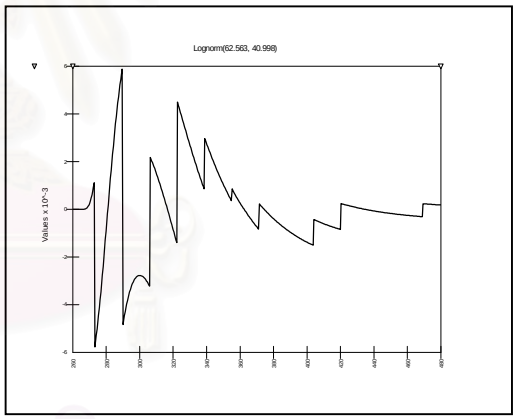
Comparison



P-P plot

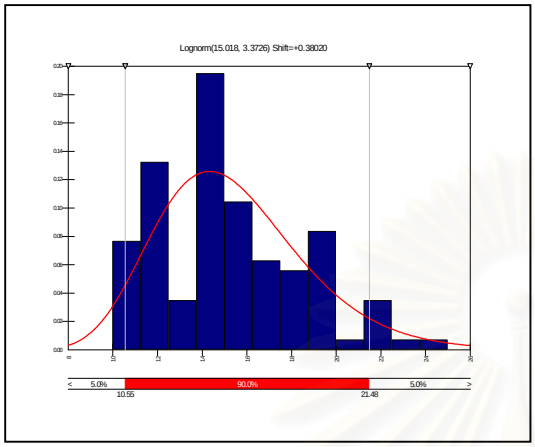


Q-Q plot

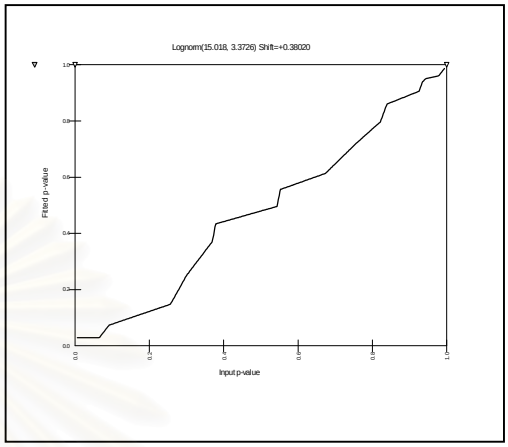


Difference

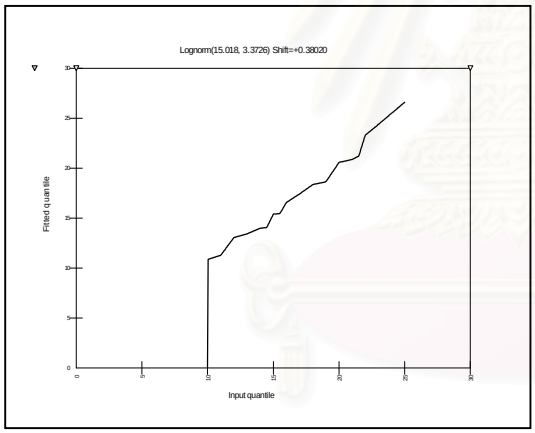
Figure A.10 Graphical distribution for intake rate of meal



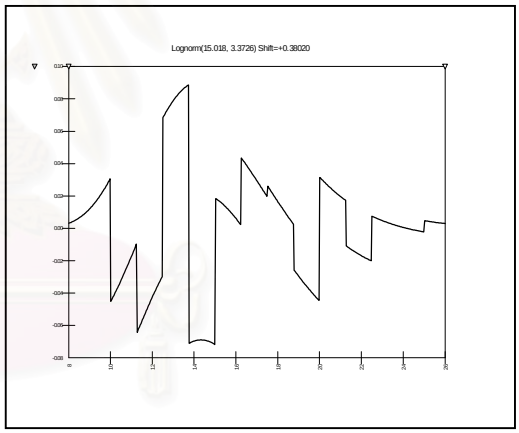
Comparison



P-P plot

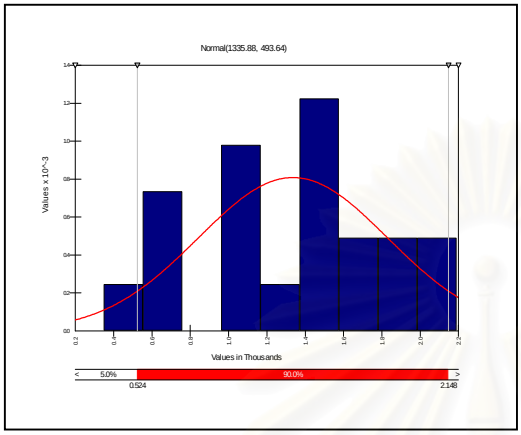


Q-Q plot

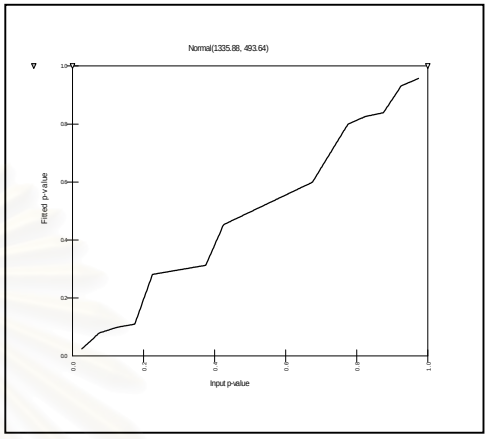


Difference

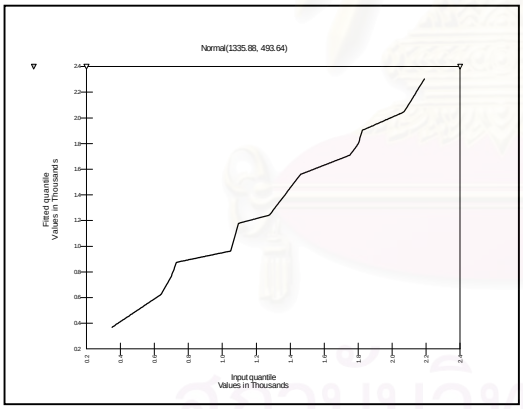
Figure A.11 Graphical distribution for body weight of children



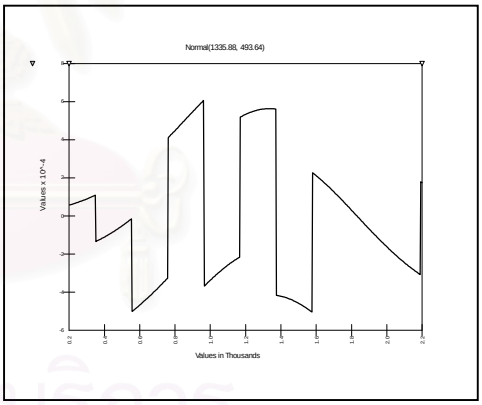
Comparison



P-P Plot



Q-Q Plot



Difference

Figure A.12 Graphical distribution for averaging time for children

Distributional Goodness of Fit

For each fit, @Risk reports one or more fit statistics. These statistics measure how good the distribution fits the input data and how confident one can be that the data was produced by the postulated probability distribution. For each of the statistics provided, the smaller the value, the better the fit. The continuous distribution parameters are estimated using Maximum Likelihood Estimator (MLE) in @RISK. The statistics used by @Risk in evaluating a fit include: Chi Square, Anderson-Darling (A-D) and Kolmogorov-Smirnov statistics (K-S). A-D statistical test.

From the results below (Table A.1), for example; the normal distribution for arsenic concentration in meal (Cm) is not rejected. The null and alternative hypothesis is formulated as follows: H_0=data is distributed normally versus H_1=data is not distributed normally. A-D test was carried out at the 95% confidence level and it fail to reject the null hypothesis.

Table A.1 Summarization table for the fitted distribution by A-D test to the sampling data

Variables	Type of distribution	Statistical test value	Critical value	Null hypothesis
Cs	Lognormal	0.3968	0.7666	Not rejected
Cm	Normal	0.5250	0.6876	Not rejected
IRm	Lognormal	0.2706	0.6392	Not rejected
BWa	Lognormal	0.5508	0.9810	Not rejected
BWc	Lognormal	1.160	1.569	Not rejected
EDa	Extvalue	0.5330	0.9069	Not rejected

Table A.1 Summarization table for the fitted distribution by A-D test to the sampling data (continued)

Variables	Type of distribution	Statistical test value	Critical value	Null hypothesis
EFa	Triangular	0.0587	0.7120	Not rejected
EFc	Triangular	0.7000	0.8921	Not rejected
ATnca	Lognormal	0.5620	0.7224	Not rejected
ATncc	Normal	0.3032	0.9002	Not rejected

Sampling method

After the data are collected and the distributions are fit to the data and the probability distributions are applied to cells containing the random or uncertain variables the model is ready for simulation. The running time over which @Risk simulates the model is either determined by the modeler or ended as a stopping rule is satisfied. In this analysis the model was simulated for ten thousand iterations. Each iterations consists of one recalculation of the model as @Risk draws random values from the distributions applied. @Risk draws random values from the underlying distributions with a procedure called sampling process. Sampling in a simulation is done repetitively, with one sample drawn every iteration from each input probability distribution. Statisticians have developed several techniques for drawing random samples. The two methods of sampling used in @Risk: Monte Carlo sampling and Latin Hypercube sampling, differ in the number of iterations required until sampled values approximate input distributions.

Monte Carlo sampling techniques are entirely random that is, any given sample may fall anywhere within the range of the input distribution. Samples are more likely to be drawn in areas of the distribution which have higher probability of occurrence. This sampling method usually requires a large number of samples to

approximate an input distribution, especially if the input distribution is highly skewed or has some outcomes of low probability.

Latin Hypercube sampling is a recent development in sampling techniques designed to accurately recreate the distribution. The Latin Hypercube technique forces the samples drawn to correspond more closely with the input distribution and thus, statistical estimates converge faster (in fewer iterations than the Monte Carlo method) on the true statistics of the input distribution. The key to Latin Hypercube sampling is stratification of the input probability distributions. Stratification divides the cumulative curve into equal intervals on the cumulative probability scale (0 to 1). A sample is then randomly taken from each interval or stratification of the input distribution. Sampling is forced to represent values in each interval and thus, is forced to recreate the input probability distribution. The technique being used during Latin Hypercube sampling is sampling without replacement. The number of stratifications of the cumulative distribution is equal to the number of iterations performed. A sample is taken from each stratification. As a more efficient sampling method, Latin Hypercube offers great benefits in terms of increased sampling efficiency and faster runtimes.

In order to shed more light on the significance of each random variable influencing the output variables, sensitivity analyses were carried out. @Risk performs sensitivity analysis based on regression or correlation analysis or both. With the regression analysis, sampled input variable values are regressed against output values which lead to a measurement of sensitivity by input variable. With the second technique, correlation coefficients are calculated between output values and each set of sampled input values. The results of sensitivity analysis can be displayed as a tornado type chart.

Simulation Results

After the simulation is completed @Risk produces the results in a separate pop-up window called the results window. This is an interactive window that is used to display the simulation results. This window includes statistics and data reports for

both the inputs and outputs of the model. Statistics generated include: the minimum, mean, maximum, and the standard deviation. Percentiles for the whole range of the input/output variables are also calculated. Percentiles are calculated in increments of five percent. @Risk offers the option to generate these reports in Excel for a better representation or modification to the modeler's preference. Some of the reports generated in this analysis are: quick simulation summary, output graphs, distributional variance and skewness.

Sensitivity Analysis

After the simulation results are obtained, it is often of interest to see which inputs have affected the outputs the greatest and by how much. @Risk produces what it is called a sensitivity report. In this report inputs that significantly affect each output cell are ranked in their respective order of significance, with the first being the one affecting output cells the most. The sensitivity analyses performed on the output variables and their associated inputs use either a multivariate stepwise regression analysis or a rank order correlation. These two methods used for calculating sensitivity analysis are discussed below:

Stepwise regression is a technique designed to calculate regression values with multiple input values. Other techniques exist for calculating multiple regressions, but the stepwise regression technique is preferable for large numbers of inputs since it removes all variables that provide an insignificant contribution from the model. At the end of each stepwise regression sensitivity report @Risk lists a goodness of fit value called the R^2 value. This value is simply a measurement of the percentage of variation that is explained by the linear relationship. If this number is less than 60% then linear regression does not sufficiently explain the relationship between the inputs and output and another method of analysis should be used (Palisade, 2005).The coefficients listed in the @Risk sensitivity report are normalized regression coefficients associated with each input. A regression value of 0 indicates that there is no significant relationship between the input and the output, while a regression value of 1 or -1 indicates a 1 or -

1 standard deviation change in the output for a 1 standard deviation change in the input.

The other technique in generating the sensitivity analysis results is the Rank Order Correlation. Correlation is a quantitative measurement of the strength of a relationship between two variables. The rank order correlation calculates the relationship between two data sets by comparing the rank of each value in a data set. To calculate rank, the data are ordered from lowest to highest and assigned numbers (the ranks) that corresponds to their position in the order. This method is preferred to linear correlation when we do not necessarily know the probability distribution functions from which the data were drawn. For example, if data set A was normal distribution and data set B was lognormal distribution, rank order correlation would produce a better representation of the relationship between the two data sets. The rank order correlation value returned by @Risk can vary between -1 and 1. A value of 0 indicates there is no correlation between variables; they are independent. A value of 1 indicates a complete positive correlation between the two variables that is when the value of the input variable is high the output value will be high. A value of -1 indicates a complete inverse relationship between the two variables when the input value samples high the output value will sample low. Other correlation values indicate a partial correlation, the output is affected by changes in the selected input, but may be affected by other variables as well. A graphical representation of the sensitivity report is obtained by generating tornado graphs. A tornado graph can be displayed for either the regression or correlation coefficients of the sensitivity analysis result. The graph represents each input variable's coefficient by a bar stretching out either to the right or to the left depending on the sign of the coefficient, positive or negative, respectively. Also, the length of the bar represents the magnitude of the coefficient, the longer the bar the higher the impact of that variable on the output cell (Palisade, 2005).

BIOGRAPHY

Piyawat Saipan was born on September 19, 1972 in Yasothon province. He received his Doctor of Veterinary Medicine from Khonkaen University in 1997. Next, he earned his Master of Science degree in Veterinary Public Health from Chulalongkorn University in 2001 and he enrolled to this university again in June 2003 for his Ph.D. in Veterinary Public Health program. Since 2006, he has been working as instructor at the Department of Veterinary Public Health, Khonkaen University, Thailand.