The Reference Value for Biomonitoring in Chemicals Risk Area in Thailand

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Abstract: The workers’ biological standard value (WBSV) is generally used to assess chemicals health risks in community. It may cause the deviate biomonitoring. Therefore, this study was aimed to set the pilot reference value for exposed people to chemicals. The study was divided into three phases: the two phases for field-study method and one phase for stakeholder’s adoption. Phase I was proceeded in one industrial zone in Thailand during the years 2012-2014 to collect blood and urine samples of 402 working-age people in community accompanied with in-depth interview. The 4 heavy metals (arsenic, cadmium, lead, mercury) in blood and urine were analyzed by atomic absorption spectroscopy (AAS) analysis and inductively coupled plasma mass spectrometry (ICP-MS). The metabolites of 4 volatile organic compounds (VOCs, benzene, toluene, styrene, xylenes) in urine were analyzed by high performance liquid chromatography (HPLC) analysis. The 8 chemicals concentrations of the volunteers’ average chemicals concentration (VACC) were calculated. Phase II was proceeded during the years 2015-2016 to compare risk group identification between usage of VACC and usage of WBSV. The results were presented in mean value, standard deviation, percentage, and significant. The results showed approximately 90 percent of VACCs were lower than WBSV. The exceptional result was volunteers’ average urinary arsenic concentration. It was clearly higher than WBSV. The comparative results showed the adjusted amount of risk people by VACC was higher than the adjusted amount risk people by WBSV. Phase III was proceeded in the year 2017 for stakeholder’s adoption. This study indicated that general people’s average chemicals concentration should be used as the reference value for biomonitoring and active health surveillance.

Key words: Reference value, biomonitoring, chemicals health risks, exposed people, active health surveillance.

1. Introduction

The biomonitoring for prevention and control of chemicals diseases always pays attention to occupational exposures because the loads of evidence show that workers expose to chemicals in their working process. The statistic data of the National Occupational Survey in the early 1980s estimated that about 30,000 workers received this occupational exposure whereas people expose a much lower level than the workers [1]. The biological monitoring was defined in a 1980 seminar, jointly sponsored by European Economic Community (EEC), National Institute for Occupational Safety and Health (NIOSH) and Occupational Safety and Health Association (OSHA) in Luxembourg as “the measurement and assessment of agents or their metabolites either in tissues, secreta, excreta, expires air or any combination of these to evaluate exposure and health risk compared to an appropriate reference” [2]. Therefore, “Biological Monitoring” is one of the three important tools in the prevention of diseases due to toxic agents [2]. Some organization, ACGIH has published guidelines known as Threshold Limit Values (TLVs®) and Biological Exposure Indices (BEIs®) for use by industrial hygienists in making decisions regarding safe levels of exposure to various chemical and physical agents found in the workplace [3]. The Threshold Limit Values (TLVs®) and Biological Exposure Indices (BEIs®) are developed as guidelines to assist in the control of health hazards in
workplace. These recommendations or guidelines are intended for use in the practice of industrial hygiene, to be interpreted and applied only by a person trained in this discipline. Because there is no safety value for people in community, the biological exposure indices (BEIs) of the American Conference of Governmental Industrial Hygienists (ACGIH) for workers in the workplace are generally used for health surveillance of the exposed people to chemicals in the environment. Actually, workers and people in community have risk to chemicals exposure from many sources. For daily life, WHO, ILO, and EPA also concern with the various sources of chemicals exposure, e.g., working process, air, water, food, and toxic chemicals [4-6]. It is found that the variables of person’s susceptibility to chemicals exposure and adverse health effects depend upon age, gender, genetics, pregnancy, and other health conditions. Therefore, biomonitoring and health surveillance are parts of continuum that can range from the measurement of agents or their metabolites in the body via evaluation of biochemical and cellular effects, to the detection of signs of early reversible impairment of the critical organ. The biological monitoring or biomonitoring for human exposure is based on the determination of indicators of the internal dose which measure the amount of chemicals in biological samples, which is composed of the initial chemicals and/or metabolites of chemicals, and concentration of chemical compounds in alveolar air [2, 6]. However, there are no biological exposure indices for people in community, particular in local people, so the workers’ biological standard value (WBSV) is generally used for risk assessment of occupational and non-occupational groups. In general, the biological indices (BEIs) by ACGIH are widely used to be the reference value for risk assessment [3, 7-11]. According to the various chemical sources in daily life, the WBSV may cause the deviate of criteria of risk assessment for biomonitoring, health surveillance, and investigation of chemicals diseases. In Thailand, since the Eastern Seaboard Development Plan has had concrete proceeding in the year 1987 by the Sixth National Economic and Social Development Plan of Thailand [12], many industrial estates have been established in the Map Tap Phut sub-district in Rayong Province. The Map Tap Phut sub-district area, locating in the central district of Rayong Province, has become the most important industrial estate area for chemical industries because of its suitable location in the eastern part of Thailand by the seashore and its convenient chemical transportation by the various logistics services, e.g., road, train, international harbour, and international airfreight [13]. The Map Ta Phut Industrial Estate has become the important area of petrochemical industries, oil refinery industries, and heavy metal industries. Because of the rapid growth of economic structure in Rayong Province, the primary main local occupation of the people has been changed from agriculture to cover the three main occupations, e.g., agriculture, industry, and service (travelling service and health service). Even though the chemicals have been possibly emitted from all occupations and the activities of daily life, the concerning with environmental effects and health effects has been generally focused on the emission of chemicals from the chemical industries, particularly in the Map Ta Phut Industrial Estate area [14]. Since the environmental effects and the health effects of chemical toxicities have been enormous number of complaints from the people in community in the year 2007, the public health officials have continuously proceeded the risk assessment and the health surveillance for biomonitoring of the workers and the local people in community by usage of the BEIs of ACGIH to identify the risk group. This method may generate the deviated results caused by the various sources of chemical exposure. Thus, the reference value of the local people was planned to be designed by application of baseline data of the average chemical concentration of general local population (non-occupations dealt with chemicals). The baseline data of the volunteers’ average chemicals
concentration (VACC) among Rayong population have been planned to be the pilot model of the reference value of risk assessment for biomonitoring and active health surveillance among the exposed people to chemicals in chemical risk area in Thailand.

2. Materials and Methods

In the year 2012, the reviewing results of the information concerning with chemicals health impacts in the whole country caused by chemicals suggested public health officials to proceed the study of the average biological concentration of the focused eight chemicals (4 heavy metals: arsenic, cadmium, lead, mercury; 4 VOCs: benzene, toluene, styrene, xylenes) among Rayong population to be the pilot study for setting the average chemical concentration in the biological samples to be the reference value for risk assessment and health surveillance of the local people who are exposed to the focused eight chemicals [15, 16]. Besides, the sources of chemicals in the Map Ta Phut Industrial Estate Authority in Rayong Province were also reviewed [16]. In the years 2012-2014, the field studies by the volunteers’ biological sampling accompanied with the questionnaires of conducting the in-depth interview were proceeded by the cooperation with the networking organizations, i.e., the two laboratories under the Division of Occupational and Environmental Diseases: (1) Rayong Occupational Health and Environmental Development Center; and (2) Reference Laboratory and Toxicology), 8 Districts Public Health Offices of Rayong Province, 19 Sub-district Health Promoting Hospitals for assisting to stratify the number of volunteers who had aged between 15-60 years (according to the labour force criteria [17-19]) in their responsible area on duty and collecting biological samples accompanied with the in-depth interview from the volunteers. The contents of the in-depth interview were covered with the consent form, the information of the general information (habitat, working history, health examination history, behavior, types of meals, and drug intake). The amount of the volunteers’ biological sampling was 402 persons (400 persons plus 2 persons who lived in the two districts adjacent to another provinces) resulted from calculating by Taro Yamane formula based on 649,275 persons in the population census of Rayong Province in the year 2012 [19, 20]. The selective sampling of the volunteers 402 persons by stratified sampling of geographical clustering of 8 districts in Rayong Province was proceeded [20]. The inclusion criteria for the volunteers were: (1) both male and female volunteers; (2) age interval was 15-60 years old; (3) Thai citizen who was one of the population census of Rayong Province; (4) having no working in the industrial workplace; (5) local people who continuously stay in Rayong Province not less than 1 year; (6) having no congenital disease and underlying disease; and (7) accepted the consent form. The exclusion criteria for the volunteers were: (1) migrant people; (2) local people who continuously stay in Rayong Province less than 1 year; and (3) having congenital disease and underlying disease. The biological samples were analyzed by the two same standardized laboratories under the Division of Occupational and Environmental Diseases (the previous name is the Bureau of Occupational and Environmental Diseases). The blood lead level, urinary total arsenic concentration level, and urinary total cadmium concentration level were analyzed by AAS analysis and the metabolites of VOCs in urine were analyzed by HPLC (high performance liquid chromatography) analysis in Rayong Occupational Health and Environmental Development Center. The urinary total mercury concentration level was analyzed by ICP-MS analysis at the Reference Laboratory and Toxicology Center. The 8 chemicals concentrations of volunteers’ average chemicals concentration (VACC) were calculated and the data accompanied with the in-depth interviewing information were interpreted. The volunteers’ age average was presented by mean value and deviation.
The average concentrations of the focused 8 chemicals in the biological samples and the risk mapping were presented. Phase II was proceeded during the years 2015-2016 by comparison of the adjusted risk group between the usage of VACC and the usage of BEIs of ACGIH in 2015 as the workers’ biological standard value (WBSV). Phase III was proceeded in the year 2017, the meeting for stakeholder’s workshop and brainstorming on health surveillance of occupational and environmental diseases have been operated in Bangkok by the Division of Occupational and Environmental Diseases. The 100 nominated representatives covering the government offices, the non-government offices, the industrial workers, the academic officials, and the local authority officials were invited to participate in the meeting. The results in mean value, standard deviation, percentage, and significant were presented.

3. Results and Discussion

The results of the reviewing of the previous information and data concerning with chemicals health impacts in the whole country caused by chemicals showed that the target risk area should be Rayong Province which was the one of the three rapidly growth economics provinces (Chonburi Province, Rayong Province, and Chachoengsao Province) under the Eastern Seaboard Development plan of Thailand which became the very important economics area in the name of Eastern Economic Corridor (EEC) since the year 1997 [7-13]. The eastern part of Rayong Province was close to Chantaburi Province, the agriculture occupation province, whereas the western part was close to Chonburi Province, the industrial occupation province. The information of the geographic profile of Rayong Province illustrated that this province locates along the eastern seashore of the gulf of Thailand which has 8 districts [15-17]. The area of the Map Ta Phut Industrial Estate in the central district of Rayong Province has been focused to be the focal point of chemicals infrastructure area including chemicals production and international chemicals import-export [16]. The enormous chemical industries, particularly in petrochemicals, oil refinery industries, and heavy metal industries have been promoted to be invested. Therefore, the three main local occupations have comprised of agriculture, industry, and service [15-19].

The geology has illustrated that this province is the mineral potential area of heavy metal, i.e., arsenic, cadmium, lead, mercury, etc. [21] (Fig. 1). Because of the emission of aromatic hydrocarbons and heavy metal from industries in the Map Ta Phut Industrial Estate Area, particular petrochemicals and refinery oil in Map Ta Phut Industrial Estate have been complained. The local people who lived surrounding the Map Ta Phut Industrial Estate requested the health protection for chemical diseases. Therefore, the active health surveillance program for people in community was yearly processed since the year 2007 and the reference value for being the standard value of the adjusted risk level of chemical concentration in the biological samples has occurred since then. For solving the lack of the reference value for the local people, the biological exposure indices (BEIs) of ACGIH for workers were used to be the standard value to identify the risk group. Because of the variety of individual’s exposure to chemicals in daily life outside of the workplace, the finding out of the standard value of the local people for adjusting the risk group will still be very important for the active health surveillance. The results of the interviewing information showed the volunteers were 135 male persons and 267 female persons. The average age of volunteers was 45 years old (SD ± 10.01). The 8 average chemicals concentrations of volunteers’ average chemicals concentration (VACC) were calculated and illustrated as followed: the blood lead level was 3.06 µg/dL, the average urinary total concentration levels of arsenic, cadmium, and mercury were 71.22 µg/L, 0.91 µg/g Cr, 4.22 µg/g Cr, respectively. The average urinary concentration level
of t,t-muconic acid (metabolite of benzene) was 191.00 µg/g Cr. The average urinary concentration level of hippuric acid (metabolite of toluene) was 379.15 mg/g Cr. The average urinary concentration level of mandelic acid plus phenylglyoxylic acid (metabolites of styrene) was 61.52 mg/g Cr, and the average urinary concentration level of methyl-hippuric acid (metabolite of xylenes) was 15.99 mg/g Cr. The results showed approximately 90 percent of VACCs were lower than WBSV and the average chemicals’ concentration level of male was significantly higher than female’s concentration \((p < 0.05)\). The other

| Type of metabolites                  | The average of 8 chemicals’ concentrations of VACC | The biological exposure indices (BEIs) of ACGIH in 2015 |
|--------------------------------------|---------------------------------------------------|--------------------------------------------------------|
| Blood lead level                     | 3.06 µg/dL                                         | 30 µg/dL                                               |
| Total arsenic in urine               | 71.22 µg/L                                         | 35 µg/L                                                |
| Total cadmium in urine               | 0.91 µg/g Cr                                       | 5 µg/g Cr                                              |
| Total mercury in urine               | 4.22 µg/g Cr                                       | 20 µg/g Cr                                             |
| t,t-muconic acid in urine            | 191.00 µg/g Cr                                     | 500 µg/g Cr                                            |
| Hippuric acid in urine               | 379.15 mg/g Cr                                     | 1,600 mg/g Cr                                          |
| Mandelic acid + phenylglyoxylic acid in urine | 61.52 mg/g Cr                                     | 400 mg/g Cr                                            |
| Methyl-hippuric acid in urine        | 15.99 mg/g Cr                                      | 1,500 mg/g Cr                                          |

VACC means the volunteers’ average chemicals concentration; ACGIH means American Conference of Governmental Industrial Hygienists.

The results of the average of 8 chemicals’ concentrations of VACC and the biological exposure indices (BEIs) of ACGIH in 2015 was shown in Table 1.

The results of the average of 8 chemicals concentration of VACC were identified into two risk mappings: (1) risk mapping of heavy metal; and (2) risk mapping of organic solvents. The risk mapping of heavy metal illustrated that the three kinds of heavy metals, e.g., lead (Pb), arsenic (As), and cadmium (Cd), were located in the area nearby Chantaburi Province in which agriculture was the main occupation whereas mercury (Hg) was located in the area nearby Chonburi Province in which industrial working was the main occupation (Fig. 2). The risk mapping of organic solvents illustrated that the three kinds of organic solvents e.g., benzene (B), toluene (T), and xylenes (X) were located in the area nearby Chantaburi Province in which agriculture was the main occupation whereas styrene (S) was located in the area nearby Chonburi Province in which industrial working was the main occupation (Fig. 2). As the pilot study, in the years 2015-2016, the VACC was used to adjust the risk group of the retrievers exposed to benzene and mercury of the crude oil spill at the shore at Koh Samet (Samet Island) on July 29, 2013, locating in Rayong Province. The two parameters of the expected, exposed to the crude oil, t,t-muconic acid (the metabolite of benzene) in urine and mercury in urine [22-24], were analyzed by the laboratory of ROHED Center for urinary mercury and urinary t,t-muconic acid by the Reference Laboratory and Toxicology Center which were proceeded for the retrievers. In the years 2013-2014, the WBSV was used to identify the risk group of benzene and arsenic exposure for health surveillance planning. In the years 2015-2016, the results of the chemicals’ concentrations of the two
parameters in the retrievers’ urine have adjusted the risk group by VACC compared with BEIs of ACGIH 2015. The adjusted risk group of 50 retrievers’ samples to mercury poisoning showed that 7 retrievers’ samples were higher than VACC whereas 3 retrievers’ samples were higher than BEIs of ACGIH 2015. The results of the adjusted risk group of 300 retrievers’ samples to benzene showed 16 retrievers’ samples were higher than VACC whereas no retriever’s sample was higher than WBSV (Table 2).

The results of VACC of the local people in Rayong Province indicated that the chemicals’ concentrations in biological sample based on the exposure in the area by the chemicals sources in the province correlated to the contamination of the mass of the heavy metals and organic solvents in the area. Besides, the heavy metal concentrations in the biological samples depended on chemicals usage in the area, i.e., urinary arsenic concentration of VACC in the area by agriculture province was higher than WBSV. The pesticides,

| Type of chemicals in retrievers’ samples | Chemicals concentration in retrievers’ samples | Retriever’s samples | Adjusted the risk number by WBSV | Adjusted the risk number by VACC |
|----------------------------------------|-----------------------------------------------|---------------------|-------------------------------|---------------------------------|
| Hg (expected exposure to mercury)       | < 0.01-45.28 μg/dL (in urine)                  | 50                  | 3                             | 7                               |
| t,t-muconic acid (expected exposure of benzene) | NA-122 μg/g Cr (in urine)                      | 300                 | -                             | 16                              |

WBSV means the workers’ biological standard value; VACC means the volunteers’ average chemicals concentration; BEIs mean biological exposure indices; ACGIH means American Conference of Governmental Industrial Hygienists.

Table 2 The comparative adjusted risk group between WBSV (BEIs of ACGIH, 2015) and VACC among the retrievers of the crude oil spill leakage shore Koh Samet (Samet Island) in Rayong Province.

Fig. 1 Mineral potential area in Rayong Province.  
Source: Department of Mineral Resources of Thailand in 2008.  
The illustrated level of severe mass (mineral ores) varied from pale color to dark color by 0-20 mass.
particularly in insecticides (organophosphorus compounds and carbamates), glyphosate-based herbicides, and rodenticides are comprised of many kinds of heavy metals [25, 26]. The Ministry of Agriculture and Cooperatives illustrated the increment of the yearly statistics of pesticides import to Thailand [24, 25]. During the years 1998-2014, the yearly statistics of pesticides import to Thailand were also increased [27, 28]. It was found that the widespread repeated exposure of the population to the pesticides and heavy metals of occupational and environmental origin and the combined effects of heavy metals and pesticides on humans through the food chain have occurred [29]. There were many study researches which indicated the distribution of contamination of heavy metals in soil and water that have been found in the area which used pesticides. Some study researches in Pakistan showed the distribution of heavy metals in the soils associated with the common use of insecticides in cotton fields in Pakistan showed the results that nickel (Ni), copper (Cu), cobalt (Co), lead (Pb), chromium (Cr) and cadmium (Cd) were respectively contaminated in the studied cotton fields [30]. Some study researches in France showed the results of the study on glyphosate-based herbicides (GBH) that the glyphosate was not the major toxic compound in the herbicide formulations whereas the petroleum-based compounds in herbicides were highly more toxic than glyphosate. Besides, the identified arsenic, chromium, cobalt, lead and nickel in pesticide formulations of glyphosate-based herbicides were found [26]. Because there were the statistics of

Fig. 2  Risk mapping of the average of 4 heavy metals’ concentrations and 4 metabolites of organic solvents of people in Rayong Province.

(1) Line  means “canal”.
(2) Abbreviation of 4 heavy metals.
As = urinary arsenic level; Cd = urinary cadmium level; Hg = urinary mercury level; Pb = blood lead level.
(3) Abbreviation of 4 metabolites of organic solvents.
B = benzene; T = toluene; S = styrene; X = xylene.
various types of pesticides use in Thailand, including in Rayong Province, the contamination of heavy metal and organic solvents based on petroleum compounds were also possibly widespread repeated exposure of the population. Therefore, the usage of VACC to identify the risk people to chemical hazards indicated the different number of the risk people. For pilot usage of VACC in the case study of oil spill attack the seashore of Koh Samet (Samet Island) in Rayong Province, in Table 2 illustrated the different number of the risk people by comparison of WBSV and VACC. If the VACC was used for identification of risk groups who were the local people in Rayong Province, the different number of risk people to chemicals will be different from WBSV usage. In the case of VACC, it was higher than WBSV, i.e., urinary arsenic concentration, which illustrated that the health effect of local people, particular in the top rank area, should be concerned to set health surveillance program for arsenic poisoning.

In the year 2017, the results from the meeting for stakeholder’s workshop and brainstorming on health surveillance of occupational and environmental diseases showed that all stakeholders (percentage was 100) adopted the VACC to be the one of health risk assessments for integrating in the health surveillance plan for the local people in the chemicals risk area.

4. Conclusions and Recommendations

The results indicated that the local people in Rayong Province have ordinary chemicals containing in their body. It might be obtained from natural source, exposure to chemicals contaminated in general environment and daily life intake. Therefore, the average of chemical concentrations in the biological samples should be used as the baseline data to be the reference value for health exposure indices of Rayong people instead of BEIs of ACGIH. According to FAO and WHO [31], the chemical substances to which humans are exposed in the environment have almost infinite number of simple, binary, tertiary and quaternary combinations. The direct experimentation has been found to be unable to resolve the risk assessment issue [29, 31]. This is the pilot model for setting the reference value for exposed people to chemicals leading to the advance process of health surveillance and investigation of chemicals diseases. Therefore, the adjusted standard value of drinking water and food intake should cover the type of hazardous chemicals which might be contaminated in food chain.

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References

[1] Institute of Medicine of the National Academies. 2014. “The Challenge: Chemicals in Today’s Society.” In Identifying and Reducing Environmental Health Risks of
The Reference Value for Biomonitoring in Chemicals Risk Area in Thailand

[Chemicals in Our Society, Workshop Summary of the Roundtable on Environmental Health Sciences, Research, and Medicine, Chapter 2. Board on Population Health and Public Health Practice. Washington, DC: National Academies Press, pp. 5-24. Assessed October 16, 2017. https://www.nap.edu/read/18710/chapter/1.]

[2] Foà, V., and Alessio, L. 2017. “Biological Monitoring.” In Encyclopaedia of Occupational Health and Safety, Part IV: Tools and Approaches, 4th ed., International Labour Office. Assessed October 16, 2017. http://www.ilocis.org/documents/chpt27e.htm.

[3] American Conference of Governmental Industrial Hygienists. 2015. TLVs® and BEIs®. The Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices, Cincinnati, OH, USA.

[4] Victorian Trades Hall Council. 2017. Hazardous Substances (Chemicals). Assessed August 31, 2018. https://www.ohsrep.org.au/hazardous_substances_chemicals.

[5] Rosenstock, L., Cullen, M., and Fingerhut, M. 2006. “Occupational Health.” In Disease Control Priorities in Developing Countries, Chapter 60, 2nd ed., edited by Jamison, T., Breman, J. G., Measham, A. R., Alleyne, G., Claeson, M., Evans, D. B., et al. UK: Oxford University Press. Assessed August 31, 2012. https://www.ncbi.nlm.nih.gov/books/NBK11750/.

[6] United States Environmental Protection Agency. 2017. “Unspecified Toxic Chemicals.” Assessed August 31, 2018. https://www.epa.gov/caddis-vol2/caddis-volume-2-source-s-stressors-responses-unspecified-toxic-chemicals.

[7] Bureau of Occupational and Environmental Diseases. 2015. Annual Report 2015. Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand. (in Thai)

[8] Bureau of Occupational and Environmental Diseases. 2016. Annual Report 2016. Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand. (in Thai)

[9] Bureau of Occupational and Environmental Diseases. 2017. Annual Report 2017. Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand. (in Thai)

[10] Bureau of Occupational and Environmental Diseases. 2018. Annual Report 2018. Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand. (in Thai)

[11] Bureau of Policy and Strategy. 2016. Public Health Statistics A.D. 2015. Ministry of Public Health, Thailand. (in Thai)

[12] Office of the National Economic and Social Development Council. The Sixth National Economic and Social Development Plan (1987-1991). Prime Minister’s Office, Thailand.

[13] Office of the National Economic and Social Development Council. The Twelfth National Economic and Social Development Plan (2017-2021). Prime Minister’s Office, Thailand.

[14] Rayong Provincial Office. 2012. “Population from Registration Record, Percent Change and Density by District: 2009-2012.” In Database of Civil Registration, Information Technology of Rayong Statistics, Department of Provincial Administration, Ministry of Interior, Thailand. Assessed January 5, 2012. http://123.242.173.8/v2/index.php?option=com_content&view=category&id=118&Itemid=217. (in Thai)

[15] Sripaung, N., Thongkumsuk, T., and Yapun, C. 2010. The Report of the Project of Pollution Solution and Quality of Life Promotion in Rayong Province in the Year 2010. Rayong Occupational Health and Development Center, Bureau of Occupational and Environmental Diseases, Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand. (In Thai)

[16] Industrial Estate Authority of Thailand (IEAT). 2012. “Environmental Impact Assessment (EIA).” Assessed January 5, 2012. https://www.ieat.go.th/eia/index.php/2013-10-27-11-09-5/4/2013-10-27-11-09-55.

[17] Rayong Provincial Office. 2012. “General Information.” In Information Technology of Rayong Province, Department of Provincial Administration, Ministry of Interior. Assessed January 5, 2012. http://123.242.173.8/v2/index.php?option=com_content&view=category&layout=blog&id=62&Itemid=135. (in Thai)

[18] National Statistical Office. 2012. The Labour Force Survey 2012. Ministry of Information and Communication Technology, Thailand. (in Thai)

[19] Rayong Provincial Office. 2012. “Population from Registration Record, Percent Change and Density by District: 2008-2012.” In Database of Civil Registration, Information Technology of Rayong Statistics, Department of Provincial Administration, Ministry of Interior. Assessed January 5, 2012. http://123.242.173.8/v2/index.php?option=com_content&view=category&id=118&Itemid=217. (in Thai)

[20] Israel, G. D. 1992. “Determining Sample Size 1.” In Fact Sheet PE0D-6. Agricultural Education and Communication Department, IFAS, University of Florida. USA. Assessed January 5, 2012. https://www.gjimt.ac.in/wp-content/uploads/2017/10/Glen-D.-Israel_Determining-Sample-Size.pdf.

[21] Department of Groundwater Resources. 2008. “Executive Summary: Project of Capacity Evaluation of Groundwater Quality, Monitoring System of
Contamination, and Groundwater Restoration Planning in Rayong Province and Chonburi Province.” Ministry of Natural Resources and Environment. Thailand. (in Thai)

[22] Simanzhenkov, V., and Raphael Idem, R. 2003. “Part I Classification and Characterization of Crude Oil.” In Crude Oil Chemistry. New York: Marcel Dekker Inc., pp. 1-67. Accessed May 5, 2014. https://books.google.co.th/books?id=om8pgoU-KiMC&printsec=frontcover&hl=th&source=gbs_ge_summary_r&cad=0#v=onepage&q&f=false.

[23] Sanchez, G. S. 2013. “Mercury in Extraction and Refining Process of Crude Oil and Natural Gas.” PhD thesis, University of Aberdeen. Accessed May 5, 2014. https://upcommons.upc.edu/bitstream/handle/2099.1/22105/Mercury%20in%20extraction%20and%20refining%20process%20of%20crude%20oil%20and%20natural%20gas.pdf?sequence=1&isAllowed=y.

[24] Hollebone, B. P. 2007. “Mercury in Crude Oil Refined in Canada.” In Emergencies Science and Technology. Division Science and Technology Branch Environment, Ottawa, Ontario, Canada. Accessed May 5, 2014. https://www.canadianfuels.ca/website/media/images/The%20Fuels%20Industry/PDF/Mercury-in-Crude-Oil-Refined-in-Canada-11Oct07.pdf.

[25] Costa, L. G. 2013. “Toxic Effects of Pesticides.” Chapter 22. In Casarett & Doull’s Toxicology: The Basic Science of Poisons, 8th ed. USA: McGraw-Hill Education. Accessed May 5, 2016. https://accesspharmacy.mhmedical.com/content.aspx?sectionid=53483747&bookid=958.

[26] Defargea, N., Spiroux de Vendómoisb, J., and Séralinia, G. E. 2018. “Toxicity of Formulants and Heavy Metals in Glyphosate-Based Herbicides and Other Pesticides.” Toxicology Reports 5: 156-63. Accessed May 5, 2019. https://www.sciencedirect.com/science/article/pii/S22147501730149X.

[27] Thai Pesticide Alert Network (Thai-PAN). 2012. “The Database of Pesticides.” In Proceedings of the Conference of Pesticides Warning, November 15-16, 2012. Accessed May 5, 2014. https://www.thaipan.org/sites/default/files/conference2555/conference2555_0_01.pdf. (in Thai)

[28] Office of Agricultural Economics. 2019. “Quantity and Value of Hazardous Agrochemicals Import (2014-2018).” Ministry of Agriculture and Cooperatives. Accessed May 5, 2018. http://www.oae.go.th/ (in Thai)

[29] Singh, N., Gupta, V. K., Kumar, A., and Sharma, B. 2017. “Synergistic Effects of Heavy Metals and Pesticides in Living Systems.” Front Chem. 5: 70. doi: 10.3389/fchem.2017.00070.

[30] Tariq, S. R., Shafiq, M., and Chotana, G. A. 2016. “Distribution of Heavy Metals in the Soils Associated with the Commonly Used Pesticides in Cotton Fields.” Scientifica. Assessed May 5, 2017. http://dx.doi.org/10.1155/2016/7575239.

[31] FAO and WHO. 2009. “Chapter No. 7 Risk Assessment.” In Principles and Methods for the Risk Assessment of Chemicals in Food Environmental Health Criteria 240. Accessed May 5, 2017. https://apps.who.int/iris/bitstream/handle/10665/44065/WHO_EHC_240_10_eng_Chapter7.pdf?sequence=10.