UNIVERSITI PUTRA MALAYSIA

HEALTH RISK ASSESSMENT OF ELECTRONIC CIGARETTE USE AMONG ADULTS IN SELECTED POPULATIONS IN THE KLANG VALLEY, MALAYSIA

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By

AZIEMAH BINTI ZULKIFLI

Thesis submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirement for the Doctor of Philosophy

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy

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May 2019

Chair : Emilia Zainal Abidin, PhD
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Introduction: Introduction: The use of electronic cigarette (EC) is a common phenomenon in Malaysia despite the lack of evidence on its potential health risks. Advertised as safer and trendy than conventional cigarette, EC has been linked with the increment prevalence of users among non-smoker population worldwide. Besides being treated as a potential harm reduction tool by the smokers, the device remain controversial in the public health context due to the presence of hazardous and carcinogenic chemicals found in the refill liquid (e-liquid) that can adversely affect the users' health. **Objective:** The overall aim of this study was to estimate the non-carcinogenic health risks due to exposure to nicotine and propylene glycol (PG) and carcinogenic health risk due to exposure to the two most potent tobacco-specific nitrosamines (TSNAs) present in locally-manufactured e-liquids, the liquid used in the EC. **Methodology:** This study was divided into three sub-studies, namely i) survey on EC use ii) chemical analysis of locally-manufactured e-liquids, and iii) health risk assessment of use of EC. This study was conducted from February 2016 until April 2017 in the Klang Valley, Selangor, Malaysia. In Sub-study I, proportion of EC users among 226 tobacco users and data on EC usage pattern were determined via a cross-sectional survey. A purposive sampling method was applied in recruiting respondents. Questionnaire distributions involved three kinds of dissemination methods which were university-based, company-based and online-based sampling approach. In Sub-study II, a total of 17 samples of the most-favored e-liquid samples which have been reported by EC users in the Sub-study I were purchased in the vape shops around the Klang Valley. The chemical analysis involved the determination of nicotine and PG contents using

gas-chromatography and the contents of two selected TSNAs (N-nitrosonornicotine (NNN) and 4-(methylnitrosamino) -1-(3-pyridyl) -1-butanone (NNK) using liquid chromatography mass-spectrometry (LC-MS/MS). Non-carcinogenic and carcinogenic health risks were estimated in the Sub-study III based on data obtained earlier. **Results:** Out of 226 of tobacco users in the Klang Valley, the results showed that the proportion of EC users was 38% (n = 86). Most users (58%) preferred the modified device which is also known as MOD type of EC. The average duration of EC use was one year with a frequency of five days a week. The preferred concentration of nicotine in e-liquids was 6 mg/mL. The reported volume of e-liquid used a day was 2 mL constituting two refills. The average levels of nicotine and PG present in locally-manufactured e-liquids were found to be 3.26 ± 1.04 mg/mL (range: 1.80-5.15 mg/mL) and 484.10 ± 98.24 mg/mL (range: 316.68-715.71 mg/mL), respectively. Nicotine was detected in all e-liquid samples declared as "nicotine-free". NNK and NNN were detected in all e-liquid samples with an average content of 0.0858 ± 0.0569 µg/L (range: 0.0160-0.1958 µg/L) and 0.3832 ± 0.2884 µg/L (range: 0.0418-0.9798 µg/L). It was estimated that the exposure to selected compounds in locally-manufactured e-liquids may pose both non-carcinogenic and carcinogenic risks to users where 2 out 10,000 of EC users face the risk of cancer. **Conclusion:** Thus, this study provided evidence on the need for a more stringent health policy in considering EC as a tool for harm reduction tool among heavy smokers and there is the need for the implementation of regulation on manufacturing and sales to prevent initiation of tobacco use among non-smoking adults to support the vision of achieving the End Game of Tobacco use by 2045.

Keywords: Electronic cigarette, e-cigarette, nicotine, propylene glycol, tobacco-specific nitrosamines, e-liquid, labelling discrepancy, health risk assessment, carcinogenic risk and Malaysia

Abstrak tesis yang dikemukan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk Ijazah Doktor Falsafah

PENILAIAN RISIKO KESIHATAN TERHADAP PENGGUNAAN ROKOK ELEKTRONIK DIKALANGAN ORANG DEWASA DI POPULASI TERPILIH DI LEMBAH KLANG, MALAYSIA

Oleh

AZIEMAH BINTI ZULKIFLI

Mei 2019

Pengerusi : Emilia Zainal Abidin, PhD
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Pengenalan: Rokok elektronik telah mendapat sambuatan yang hebat di Malaysia walaupun kekurangan bukti tentang potensi risiko kesihatan peranti tersebut. Diiklankan sebagai lebih selamat dan bergaya berbanding rokok konvensional, rokok elektronik telah dikaitkan dengan peningkatan prevalen pengguna dikalangan populasi bukan perokok di seluruh dunia. Selain di anggap sebagai alat pengurang kemudaratan oleh perokok, peranti ini kekal kontroversi dalam kontek kesihatan awam kerana kehadiran bahan kimia berbahaya dan karsinogen yang dikesan di dalam cecair isi semula *(e-liquid)* dan wap air rokok elektronik yang boleh memberi kesan buruk kepada kesihatan pengguna. **Objektif:** Tujuan utama kajian ini adalah untuk menganggarkan i) risiko kesihatan bukan karsinogenik akibat pendedahan kepada nikotin dan propalina glikol (PG) dan ii) risiko kesihatan karsinogenik akibat pendedahan kepada dua *tobacco-specific nitrosamines (TSNAs)* yang terdapat di dalam produk cecair rokok elektronik tempatan. **Metodologi:** Kajian ini terbahagi kepada tiga sub-kajian, iaitu i) Tinjauan terhadap penggunaan rokok elektronik, ii) analisis kimia cecair rokok electronik tempatan, dan iii) penilaian risiko kesihatan terhadap penggunaan rokok elektronik. Kajian rentas keratan ini telah dijalankan dari Februari 2016 hingga April 2017 di Lembah Klang, Selangor, Malaysia. Dalam sub-kajian I, kadar prevalen pengguna rokok elektronik dikalangan 226 pengguna tembakau dan data corak penggunaan rokok elektronik telah ditentukan melalui tinjauan keratan rentas. Kaedah persampelan *purposive* telah digunakan dalam pengambilan responden. Pengagihan soalan kaji selidik melibatkan tiga kaedah; soal selidik berasaskan universiti, soal selidik berasaskan syarikat dan soal selidik atas talian. Dalam sub-kajian II, sebanyak 17 sampel cecair rokok elektronik tempatan yang paling digemari oleh pengguna rokok elektronik yang dilaporkan dalam sub-kajian I, telah dibeli di kedai-kedai di sekitar Lembah Klang, Selangor. Semua sampel telah dianalisa untuk

penentuan kepekatan nikotin dan PG menggunakan gas kromatografi dan kandungan dua jenis *TSNAs* [*(N-nitrosonornicotine*, (*NNN)* dan *4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)*] menggunakan *liquid chromatography mass-spectrometry* (LC-MS/MS). Dalam sub-kajian III, risiko bukan karsinogenik dan karsinogenik dianggarkan berdasarkan data yang diperoleh sebelum ini. **Hasil kajian:** Daripada 226 orang pengguna tembakau di Lembah Klang, keputusan menunjukkan bahawa perkadaran pengguna rokok elektronik adalah 38% (n = 86). Kebanyakan pengguna (58%) cenderung untuk menggunakan rokok elektronik jenis MOD. Purata tempoh masa penggunaan rokok elektronik adalah setahun dengan kekerapan lima hari seminggu. Kepekatan nikotin yang paling digemari oleh pengguna adalah 6 mg/mL. Jumlah penggunaan isipadu cecair rokok elektronik dalam sehari yang dilaporkan adalah 2 mL dengan dua kali isian. Tahap purata nikotin dan PG yang terkandung di dalam cecair rokok elektronik tempatan masing-masing adalah 3.26 ± 1.04 mg/mL (julat: 1.80-5.15 mg/mL) dan 484.10 ± 98.24 mg/mL (julat: 316.68-715.71 mg/mL). Kandungan nikotin adalah dikesan di dalam semua sampel cecair rokok elektronik yang dilabel sebagai "bebas nikotin". *NNK* dan *NNN* dikesan di dalam semua sampel cecair rokok elektronik dengan purata 0.0858 ± 0.0569 μg/L (julat: 0.0160-0.1958 μg/L) dan 0.3832 ± 0.2884 μg/L (julat: 0.0418-0.9798 μg/L). Adalah dianggarkan bahawa pendedahan kepada nikotin, PG dan *TSNAs* dalam cecair rokok elektronik tempatan boleh menimbulkan risiko bukan karsinogenik dan karsinogenik kepada pengguna. Pengiraan risiko kanser menunjukkan bahawa dua daripada 10,000 pengguna rokok elektronik dianggarkan menghadapi risiko kanser akibat rokok elektronik. **Kesimpulan:** Oleh itu, kajian ini telah membuktikan bahawa perlunya kepada dasar kawalan tembakau yang ketat dalam mempertimbangkan rokok elektronik sebagai peranti bagi mengurangkan kemudaratan kesihatan dikalangan perokok tegar dan keperluan untuk pelaksanaan peraturan pembuatan dan penjualan cecair rokok elektronik. Ini perlu bagi mencegah penggunaan tembakau dikalangan orang yang tidak merokok dalam usaha menyokong visi untuk mencapai *End Game* penggunaan tembakau pada tahun 2045.

Kata kunci: Rokok elektronik, e-rokok, nikotin, propalina glikol, *Tobacco-specific Nitrosamines*, cecair rokok elektronik, percanggahan pelabelan, penilaian risiko kesihatan, risiko kanser, dan Malaysia

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the Doctor of Philosophy. The members of the Supervisory Committee were as follows:

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ADD	Average daily dose
ATC	Averaging time for cancer
ATNC	Averaging time for non-cancer
ATSDR	Agency for Toxic Substances and Disease Registry
BW	Body weight
CC	Conventional cigarette
CSF	Cancer slope factor
DNA	Deoxyribonucleic acid
EC	Electronic cigarette
ED	Exposure duration
EF	Exposure frequency
ENDD	Electronic nicotine delivery device
ESI	Electrospray Ionisation
US FDA	United States Food and Drug Administration
GC-FID	Gas Chromatography-Flame Ionisation Detector
GRAS	Generally recognised as safe
HPLC	High Performance Liquid Chromatography
HQ	Hazard quotient
HQ_i	Hazard quotient for individual compound
HQ_T	Total hazard quotient
HRA	Health risk assessment
IARC	International Agency for Research on Cancer
IR	Ingestion rate
ITC	International Tobacco Control
IPH	Institute of Public Health
LADD	Lifetime average daily dose
LC-MS/MS	Liquid Chromatography-Mass Spectrometry and Liquid Chromatography-Tandem Mass Spectrometry
LCR	Lifetime cancer risk
LCR_i	Lifetime cancer risk for individual compound
LCR_T	Total lifetime cancer risk
MOD	Modifiable device
MOH	Ministry of Health
MOSTI	Ministry of Science and Technology and Innovation
NAB	N-Nitrosoanabasine
NAT	N-Nitrosoanatabine
NECS	National Electronic Cigarette Survey
NNA	4-(Methylnitrosamino)-4-(3-pyridyl) butanal
NNAL	4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanol
NNK	4-(Methylnitrosoamino)-1-(3-pyridyl)-1-butanone
NNN	N-Nitrosonornicotine
NSPTC	National Strategic Plan for Tobacco Control
PG	Propylene glycol
RfD	Reference dose
RSD	Relative standard deviation
TECMA	Tobacco & E-cigarette Survey among Malaysian Adolescent
TSNAs	Tobacco-specific nitrosamines

UK	United Kingdom
USA	United States of America
US DHHS	United States Department of Health and Human Services
USEPA	United States of Environmental Protection Agency
WHO FCTC	World Health Organization Framework Convention for Tobacco Control
WHO	World Health Organization

CHAPTER 1

INTRODUCTION

1.1 Electronic Cigarette (EC)

The World Health Organization (WHO) defines electronic cigarette (EC) as a battery-powered electronic nicotine delivery device (ENDD) that resembles the function of a conventional cigarette (WHO, 2009; Pataka & Argyropoulou, 2012). According to Bullen and colleagues (2010), EC provides nicotine in the form of vapour, which is inhaled into the mouth and upper airways, similar to a cigarette. The act of inhaling through or "vaping" will transform the liquid into vapours (Dawkins, Turner, Roberts, & Soar, 2013).

1.2 History and Timeline of EC Emergence

The electronic cigarette (EC) was invented by Hon Lik in 2003, a Chinese pharmacist, and had been marketed in China as a smoking cessation device since 2004 (Willershausen et al., 2014; Yamin, Bitton, & Bates, 2010). It was developed and patented by a China-based Company, Ruyan Group (Holding) Limited in Beijing, China. In 2006, the EC, which were touted as an alternative for smokers to reduce or stop smoking, was launched into the European and American market. Since then, it has been going through rapid growth in type, design, and overall engineering characteristic (Grana, Benowitz, & Glantz, 2013; Bhatnagar et al., 2014; Brown & Cheng, 2014). In early 2014, about 466 ECs' brands and 7764 flavours of EC were available in the market (Bhatnagar et al., 2014; Zhu et al., 2014). On September 2008, the WHO media center released their stand on EC stating that international health body did not prove EC as another kind of nicotine replacement therapy or smoking cessation aid (WHO, 2008). Meanwhile, in 2009, EC was introduced into the Malaysian market. The acceptance of the device among the local population soared exponentially despite the uncertainty on its safety (Gravely et al., 2014; Palipudi et al., 2016). The timeline of the emergence of EC across countries is summarised in Figure 1.1, starting from its first invention in 2003 until 2009, when the device entered the Malaysian market.

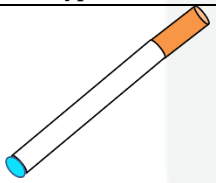
1.3 Evolution of EC

The EC has gone through a rapid product engineering evolution with modifications on the specification of its structure, battery voltage, and varied volume of e-liquid in a product. Table 1.1 summarises the evolution of EC from the 1st to the 3rd generation of EC (Farsalinos & Polosa, 2014; Grana et al., 2014). Having a cigarette-shaped, plastic or metal device, the first generation of EC is made of a battery, a reservoir for EC solution or "e-liquid", and a fibrous material where the solution is placed on, called atomiser. This device is not rechargeable or refillable, and it is to be discarded after the device stop producing an aerosol.

The second generation of EC was introduced with a cartridge that combined the e-liquid reservoir with wick/fiber and heating element into a single unit, called a cartomiser (Farsalinos et al., 2014a). Cigarette-shaped and sized, it comes with a high capacity lithium battery and tank atomiser, giving it the capability to be re-filled with e-liquid (Farsalinos et al., 2014a). This type of EC is rechargeable and often includes a feature that regulates puff duration and the number of puffs that can be consecutively taken (Grana et al., 2014).

The third generation of EC is a medium-sized device and has a higher capacity battery (Grana et al., 2014). It is also known as a "MOD" representing modification due to the device being modifiable. The unique features of the third generation of EC include having a manual switch and a battery casing. These are installed to customise the battery's capacity. The size is much larger than a conventional cigarette, and it includes a large refillable cartridge.

Table 1.1: Evolution of EC (Source: Farsalinos & Polosa, 2014; Grana et al., 2014)

Type of EC	Descriptions
 First generation	• Cigarette-shaped device • Consist of: i) small lithium battery: may be disposable ii) cartomizers; cartridge containing atomiser, pre-filled with e-liquid • Not-rechargeable or re-fillable
 Second generation	• Cigarette-shaped device • Consist of: i) high capacity of lithium battery: ii) atomiser; has capability to be re-filled with e-liquid • Often contains an element: regulate puff duration or number of puffs may be drawn consecutively
 Third generation	• Much larger than conventional cigarette • Known as "MOD': modifications • Consist of: i) higher capacity battery with integrated circuits; modifiable in term of voltage and power to be delivered to atomiser ii) larger re-fillable cartridge • Contains manual switches, a battery casing for customizing battery capacity • Can be easily modified

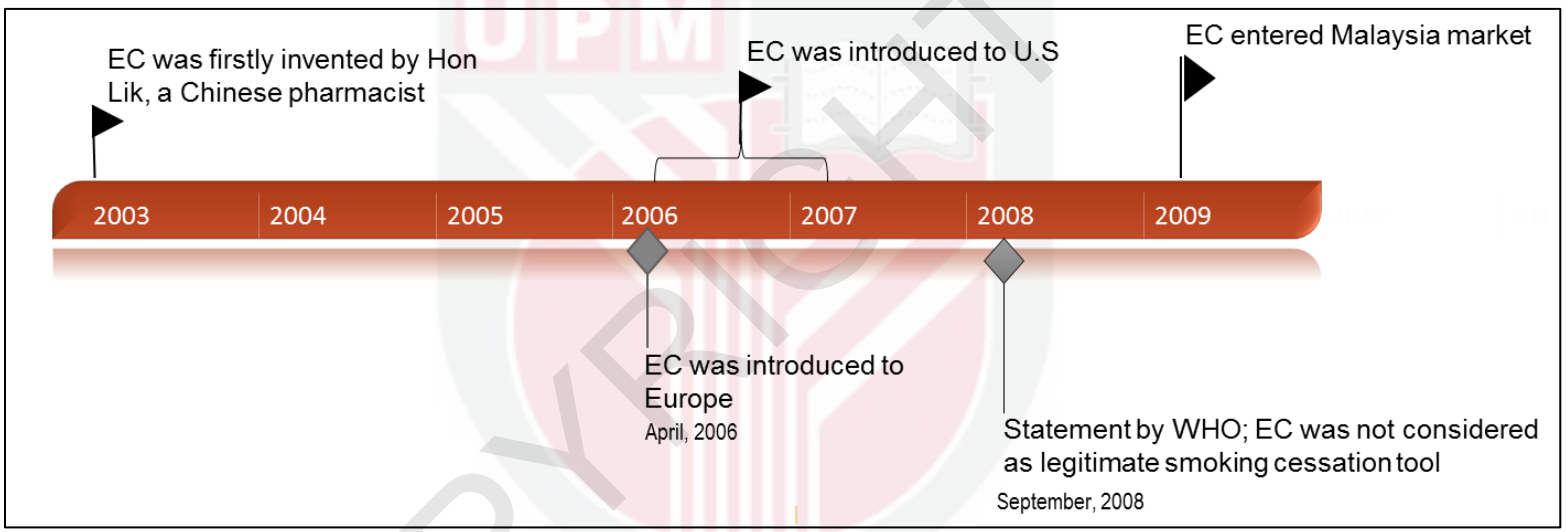


Figure 1.1: Timeline of EC emergence across countries (Source: WHO, 2008; Grana, Benowitz, & Glantz, 2013; Willershausen et al., 2014; Bhatnagar et al., 2014)

1.4 Components of EC

Regardless of its engineering invention, EC comprises three essential basic components; 1) a rechargeable battery, 2) a cartridge containing e-liquid, and 3) an atomiser, the electronic vapourisation system (WHO, 2009) which includes a vapourisation chamber with a heating element (Bertholon, Becquemin, Annesi-Maesano, & Dautzenberg, 2013; Bhatnagar et al., 2014). Figure 1.2 shows the components of the 3rd generation of EC. Meanwhile, the third generation EC is equipped with drip tip; where the users will inhale the vapour, glass tube; filled with e-liquid, cotton coil with heating element, metal base; where air flow controller is located, control buttons: include manual switches to operate the device, and battery compartment which locates the rechargeable batteries.

The principle of EC operation is to deliver nicotine in the form of an aerosol. It is puffed in a similar way to a regular cigarette. When a sensor detects airflow, it activates a heating element that is in contact with the cartridge containing nicotine solution. Then, when temperature and airflow increase, e-liquid (either nicotine-free or nicotine-contained) is vapourised and aerosol with droplets of the solution is generated. This is then inhaled by the vapers (Pauly, Li, & Barry, 2007; Wollscheid & Kremzner, 2009; Cahn and Siegel, 2010; Henningfield & Zaatari, 2010; Etter, Bullen, Flouris, Laugesen, & Eissenberg, 2011; Goniewicz, Lingas, & Hajek, 2013a).

Figure 1.2: Components of EC

1.5 International Organisations' Positions on EC

The emergence of EC has become a controversial issue among public health practitioners and policy makers; whether the potential benefits have outweighed its harmful effects to users. In addressing the issue, a few different positions regarding the use of EC either for smoking cessation or as a gateway to other tobacco products have been issued by multiple international medical and regulatory bodies.

In 2016, the World Health Organization (WHO) has announced their stand on the issue of EC in a report of the Conference of the Parties (COP) to the WHO Framework Convention on Tobacco Control (WHO, 2016). The organisation did not established EC as a smoking cessation tool due to insufficient evidences on the efficacy of EC in promoting cessation among smokers. Similar position has been revealed by the Centers for Disease Control and Prevention (CDC), which had resisted the use of EC as another kind of tool in a smoking cessation approach (Chu, Sidhu, & Valente, 2015). In addition, the European Respiratory Society recommending against the use of EC as a quit smoking aid due to insufficient evidence of controlled clinical trials to support the decision. As there is inadequate literature on the long-term health effects of EC use, therefore, no concrete conclusion can be drawn whether the device is safer than conventional cigarette (Bals, 2019).

However, a contradictory position has been announced by multiple international health agencies. The Public Health England has recommended the use of EC among smokers who intended to quit smoking (McNeill et al., 2015; Green, Bayer & Fairchild, 2016; Ghosh & Drummond, 2019). The harm reduction approach of EC has been supported by the Public Health England when the organisation has revealed that EC was estimated to be 95% safer than conventional cigarette (McNeill et al., 2015).

1.6 The EC Regulation in Malaysia

Malaysia has been a member of the World Health Organization Framework Convention on Tobacco Control (WHO FCTC) agreement since September 23, 2003 (WHO, 2017). As a member of this agreement, Malaysia is responsible to strengthen the implementation and enforcement of tobacco control regulation and policy in order to protect the public's health from the devastating effects of tobacco exposure. In Malaysia, the main regulation on tobacco control is under the Control of Tobacco Product Regulations 2004; a sub-regulation of the Food Act 1983 (Malaysia Food Act, 1983). Following the controversial issue on the EC in Malaysia in 2015, the regulation has been amended, particularly on the definition of "smoking" in the Control of Tobacco Product (Amendment) (No. 2) Regulations 2015 (Control of Tobacco Product Regulations, 2015). This step was taken to include EC under this regulation.

In addition, the National Strategic Plan for Tobacco Control (NSPTC) (2015-2020) was published in the same year by the Ministry of Health Malaysia (MOH) (MOH, 2015a). In fulfilling a commitment towards WHO FCTC agreement as well as in reaching a Global

Non-Communicable Disease Target by 2025, a national policy was outlined in this strategic plan to shape Malaysia into a smoke-free nation by 2045. The NSPTC (2015-2020) is made of four strategic plans including i) strengthening the existing tobacco control activities, ii) strengthening the legislation and enforcement of national tobacco control, iii) empowering the involvement of public and multi-sectoral agencies, and iv) strengthening tobacco control activities via MPOWER strategy. The MPOWER is the policy package introduced by the WHO, specifically for tobacco control (MOH, 2016). The strategies outlined in this plan were aimed to diminish the tobacco demand in the country level by including five key facts which were; i) "M" for monitor tobacco use, ii) "P" for protecting people from tobacco use, iii) "O" for offering help to quit smoking, iv) "W" for warning about danger of tobacco use, v) "E" for enforcing bans on advertising, promotion and sponsorship of tobacco and vi) "R" for raising tobacco taxes.

Furthermore, with regards to EC's widespread use and sale in the local market a few years back, the official press statement by MOH Malaysia was released in December 2015 pertaining to the government's stand on EC-related issue (MOH, 2015b). The use and sale of nicotine-containing EC are subjected by the rules and regulations of the Malaysian Food Act 1983 (Control of Tobacco Product Regulations 2004) and the Poison Act 1952. As stated by the MOH, the organisation is inclined towards prohibiting the EC as proposed by the WHO FCTC and the International Union Against Tuberculosis and Lung Disease (IUJTLD) (MOH, 2015b). This proposition is valid until adequate evidence of its benefits outweighs its harmful effects. Also, following the announcement of the National Fatwa Council on the prohibition of EC use among the Muslim population, the state governments of Johor and Kelantan have declared a ban on EC use in both states (The Star Online, 2015a; The Star Online, 2015b).

At the end of 2016, the Malaysian government has taken a further step in regulating EC. Three ministries – the Ministry of Domestic Trade and Consumer Affairs (formerly known as Ministry of Domestic Trade, Cooperatives and Consumerism), the Ministry of Health (MOH), and the Ministry of Energy, Science, Technology, Environment & Climate Change (formerly known as Ministry of Science, Technology and Innovation) – were tasked to regulate the use of EC as follows:

i) The Ministry of Domestic Trade and Consumer Affairs

   a) To enforce and regulate safety standards for EC devices, batteries, and other EC's components [Consumer Protection Act 1999 (Act 599)]
   b) To enforce and regulate the labelling of EC devices, nicotine-free liquid, and vapes [Trade Descriptions Act 2011 (Act 730); the Price Control and Anti-Profiteering Act 599 (Act 723) and the Weights and Measures Act 1972 (Act 71)]

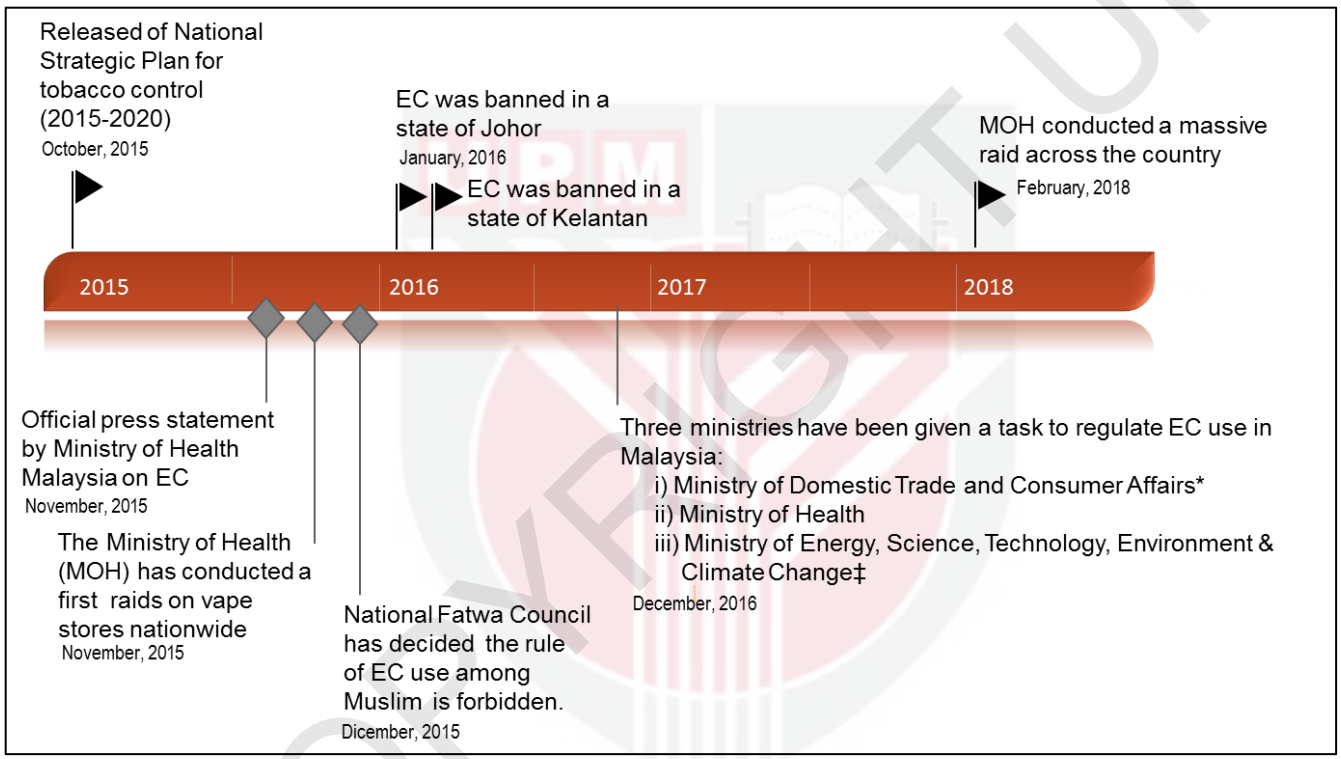
ii) The Ministry of Health (MOH)

a) To regulate the sale of nicotine-containing e-liquid (Poisons Act 1952 and Sale of Drugs Act 1952)
b) To regulate the sale, promotion, and use of health-related labelling for nicotine-free e-liquid product

iii) The Ministry of Energy, Science, Technology, Environment & Climate Change

a) Responsible for development standards of EC batteries, other EC components, and nicotine-free e-liquid's packaging (Standards of Malaysia Act 1996)

Figure 1.3 demonstrates the timeline for the implementation of EC-related regulations in Malaysia. It summarises the actions taken by the Malaysian authorities in handling EC-related issues on the state and national level. In addition, it commenced with the establishment of the National Strategic Tobacco Control Plan 2015-2020 at the national level, followed by the release of a press statement by the Ministry of Health Malaysia regarding the government's stand on the EC issue at the end of 2015 (MOH, 2015a; MOH, 2015b). In early 2016, a few states' governments started to show their commitment to control the use of EC among their state's citizen by banning its use (The Straits Times, 2015). A further step was taken by the government by delegating the tasks of managing EC devices to three ministries.



(= formerly known as Ministry of Domestic Trade, Cooperatives and Consumerism; ‡= formerly known as Ministry of Science, Technology and Innovation)*

Figure 1.3: Timeline of implementation and enforcement of EC-related regulations in Malaysia (Source: MOH, 2015a; MOH, 2015b; The Straits Times, 2015)

1.7 Problem Statement

Smoking has become a major public health concern because it has been linked with various morbidities and mortalities among world population. Within the context of Malaysia, about 10,000 deaths associated with smoking-related diseases are reported annually and it has become the major contributor to disability-adjusted life years (DALY) and lost years of life (IPH, 2004; IPH, 2011; Lim et al., 2018). According to the National Health and Morbidity Survey (NHMS) 2015, the prevalence of current smokers in Malaysia was 22.8% where it was estimated that approximately five million of Malaysian people aged 15 years and above smoked. This survey was done among nationally-representative samples of 30,000 Malaysian populations (IPH, 2015). The proportion of male smokers was higher than female, where male smoking accounted for 43% (versus 1.4% among females). However, the findings revealed the increment of prevalence of female smokers; from 1.0% in 2011 to 1.4% in 2015. The existence of innovative tobacco products such as EC has challenged the effort on anti-smoking campaigns implemented by the government.

The National Electronic Cigarette Survey (NECS 2016) has reported that the prevalence of current EC users among adult population in Malaysia was 3.2% which accounted for 600,000 users nationwide. In addition, evidences from international studies reveals that the popularity and prevalence of EC usage were increasing rapidly among the world population, including Malaysia (Dockrell, Morrison, Bauld, & McNeill, 2013; Czoli et al., 2014; Li et al., 2015; Palipudi et al., 2016). The finding by the International Tobacco Control (ITC) project conducted in 10 countries on awareness, trial, and current use of EC showed that Malaysia was one of the countries with the highest prevalence of current EC user, accounted for 14% of the total sample size (Gravely et al., 2014). This issue is worsening when multiple studies shown a high prevalence of dual users among Malaysian population, which accounted between 10.4% (Palipudi et al., 2016) to 15% (Gravely et al., 2014). This raises legitimate concern regarding the use of EC, which was advertised, as a harm reduction tool among smokers without proper scientific backing.

The absence of local usage patterns data on EC among Malaysia population has restrained policymakers from drafting regulations, standards or guideline to manage this issue wisely. Usage patterns data is crucial because previous studies have usefully demonstrated the variety of patterns across the countries (Etter, 2010; Behar, Hua, & Talbot, 2015). In addition, usage patterns data will include usage duration, usage frequency, number of puffing per day, and volume of e-liquid used in a day. By knowing the EC usage patterns or topography of local users, it may facilitate a comprehensive health risk assessment (HRA) to be performed.

Apart from that, multiple evidence has shown that there are hazardous chemical contents in EC (Hutzler et al., 2014; Famele et al., 2015; Tierney, Karpinski, Brown, Luo, & Pankow, 2015). The US FDA claims that EC contains carcinogens and toxic chemicals such as nitrosamines which can adversely affect human health (Westenberger, 2009). The statement was supported by various studies focusing on the chemical contents of e-liquids such as nicotine, TSNAs, and carbonyl compounds

(Goniewitz et al., 2013b; Etter et al., 2013; Kim & Shin, 2013). For example, tobacco-specific nitrosamines (TSNAs), the most potent carcinogenic compounds in tobacco product, have been detected in e-liquids samples on average of 1.71 (1.69) µg/L for 4-(methylnitrosamine)-1-(3-pyridyl)-1-butanone (NNK) and 4.06 (9.34) µg/L of N-nitrosonornicotine (NNN) (Kim & Shin, 2013). These data proved that EC users might be exposed to various hazardous chemicals that may possibly cause health effects.

Currently, there is no available standard or guideline for the manufacture and production of local e-liquids. Thus, the quality and safety of e-liquids produced locally should be verified. Several studies conducted in other countries demonstrated labelling discrepancy of e-liquids with regard to nicotine concentration (Goniewicz et al., 2013b; Cheng, 2014; Kim, Goniewicz, Yu, Kim, & Gupta, 2015). Furthermore, the analysis of e-liquids/EC cartridges revealed some irregularities from the actual nicotine content. In other words, the concentration measured did not correspond to the label on the product. Many studies have reported that smokers perceived EC as a smoking cessation tool (Etter, 2010; Barbeau, Burda, & Siegel, 2013). Therefore, the inaccurate labelling of nicotine content in the e-liquids products will either lead to overconsumption or insufficient dose of nicotine. This may prolong the user's nicotine addiction, contradicting with its aim of smoking cessation.

Furthermore, the health risk concern raised by the WHO pertaining to the use of EC was highlighted in the Technical Report Series 955 in 2009. The WHO states that the safety of ECs is not ensured (WHO, 2008). Nevertheless, there have been different views on the safety of EC reported, with users claiming the product is safer and less toxic than a conventional cigarette (Etter, 2010). It is worsened by the abundance of EC and locally-manufactured e-liquids in the local market, with at least 600 vape shops nationwide and more than 400 locally-manufactured MOD and e-liquids brands (The Star Online, 2015; Hutt, 2016). Following this, the users might be exposed to the unknown health risk, particularly carcinogenic and non-carcinogenic health effects. Currently, there has been no health risk assessment performed among local EC users who use local e-liquids that is not subjected to any specified standards on its contents and quality assurance. The device has been widely used as a harm reduction tool without any scientific or health risk assessment proves.

1.8 Study Justification

The worldwide increase of EC user implies the possibility of the same situation in Malaysia. The data in the ITC report conducted from 2010 till 2012 regarding EC users in Malaysia (14%, n = 280) may possibly double as demonstrated by other countries [United Kingdom = 2012 (8.9%, 95% Confidence Interval (CI) 7.0 - 10.8); 2014 (15.5%, 95% CI 12.9 - 18.0), and France = 2012 (7.3%, 95% CI 5.7 - 9.0); 2014 (21.3%, 95% CI 18.3 - 24.3)] (Gravely et al., 2014; Filippidis, Laverty, Gerovasili & Vardavas, 2017). Thus, it is important to continually monitor the local situation pertaining to the usage of EC for updated information on the latest prevalence of EC usage. This is in line with one of the strategies in the NSPTC (2015-2020) outlined by the WHO FCTC, which is to monitor (M) the tobacco use among the population. To

some extent, this study will provide the current proportion of EC users among adult tobacco users. Therefore, this study could provide the authorities with the current trend of EC use for the best measures in controlling its usage, specifically among young generation and non-smokers.

Apart from that, the high use of EC among Malaysian population has urged the need for EC usage topography data of local users. For instance, the data on EC usage topography pattern will include the information usage duration, the daily amount of e-liquid used, and usage frequency in a day. Although there have been studies identifying the usage patterns of EC, this study is tailored for EC usage topography practised by Malaysian adult users. The data are important in estimating the health risk that may be encountered by local users raised or affected by their usage patterns of EC.

Furthermore, analysis of various hazardous chemical compounds in e-liquids manufactured in other countries warranted such analysis for local e-liquid products. Chemical analysis is crucial in assisting the government in drafting any standards, guideline or regulation regarding EC. Any decision taken by the government or other related authorities will hold better if it is supported by scientific evidence. Therefore, a chemical analysis, including determination of nicotine, PG, and selected TSNAs concentration contained in locally-manufactured e-liquids should be performed. This will be beneficial for the policymakers in supporting any decision taken to control the tobacco use among the Malaysian population.

The issue of having no standards or guideline for e-liquids production has shown the importance of conducting chemical analysis on locally-manufactured e-liquids. Furthermore, it is clearly stated in one of the NSPTC (2015-2020)'s mission that Malaysians who are born from 2009 onwards will be less likely to initiate smoking. To assist the government, any new form of nicotine delivery device such as EC that resembles the function of conventional cigarette in delivering the nicotine should be monitored (via enforcement and standards/guideline). This is in terms of its contents and is executed to avoid any potential initiation of nicotine addiction among the younger population.

In addition, a comprehensive HRA must be performed to estimate the health risk encountered by local users resulted from the current pattern of EC usage in Malaysia and the chemical contents of the most favoured locally-manufactured e-liquids. In addition to providing scientific evidence via mathematical estimation of health risk that may potentially be exposed to the local users, the finding of HRA could reinforce the notion that EC is not as harmless as advertised. By providing such information to the local public especially the adolescents [≤ 14 years old: age of smoking initiation among Malaysian adolescents (IPH, 2017)], the message can be received at an early age, preventing the initiation of tobacco use in the future. Therefore, this study will assist the government in achieving one of the indicators of Global Target of Non-Communicable Disease 2025 related to smoking – decreasing 30% of smoking prevalence by 2025. In accomplishing the vision, the Ministry of Health has drafted two programs includes activities that prevent the initiation of smoking among non-smoker citizens and rehabilitation activities and enforcement to ensure at least 130,000

smokers quit smoking every year (MOH, 2015a). Delivering a message on hazardous effects of smoking and tobacco at an early age may prevent the initiation of smoking and vaping at a later age. This will consequently support the governments' initiative as stated in the NSPTC (2015 – 2020) to shape a Smoke-Free Malaysia (The End Game) by 2045. The End Game for tobacco is a national target to achieve of less than 5% of smoking prevalence by 2045, in line with the Malaysia's commitment to the WHO Framework Convention on Tobacco Control (WHO FCTC) (MOH, 2016).

1.9 Conceptual Framework

Figure 1.4 presents the conceptual framework of the study. This study mainly focused on the EC, one of the aerosolised tobacco devices. Also known as electronic nicotine delivery device (ENDS), an EC was created to imitate the function of conventional cigarette in delivering nicotine and other chemicals in the form of vapour.

The device has gained attention from the adult population particularly among smokers; when it was initially marketed as a safer alternative tool to the conventional cigarette (Chun, Moazed, Calfee, Matthay & Gotts, 2017). Therefore, current or former adult smokers who used EC among selected populations in Klang Valley, Selangor were the main target group to be recruited in the study. Multiple studies have shown that there was a rapid increase of EC users among the populations (Dockrell et al., 2013; Dawkins et al., 2013). Moreover, a survey by the International Tobacco Control (ITC) conducted in 2011/2012 in Kedah, Terengganu, Johor and Selangor demonstrated that the prevalence of current users of EC was higher in Malaysia compared to China, the UK, the US, Canada, the Republic of Korea, Mexico, Brazil, Australia, and the Netherland (Gravely et al., 2014). Therefore, this study was conducted to update the information on current baseline data, particularly among adults in Klang Valley, Selangor.

Moreover, e-liquid was the main source of chemical exposure to EC users as it contained nicotine, PG, heavy metals, carbonyls and another hazardous chemical such as TSNAs (Kim & Shin, 2013; Farsalinos, Kistler, Gillman, & Voudris, 2014c; Farsalinos et al., 2015a; Farsalinos, Gillman, Poulas, & Voudris, 2015b; Farsalinos, Voudris, & Poulas, 2015c).

In this study, there were four kinds of chemicals which have been determined in terms of its contents and health risk towards the users; namely nicotine, PG, NNN and NNK. Nicotine is widely known as an addictive agent contained in most of other tobacco products, which functions to retain the usage (US DHHS, 1988). Even though PG has been mostly used in other industries, the big concern is the uncontrolled application of the compound in the production of e-liquids that may be harmful to health (Kienhuis et al., 2015). In addition, TSNAs is the major cancer causative agent in most of the tobacco products (Hecht, 1998). In addition, the strongest carcinogen of TSNAs, namely NNN and NNK (IARC, 2012) were also highlighted in the chemical analysis of locally-manufactured e-liquids.

Within the regional context, there was an abundance of locally manufactured e-liquid products available in Malaysian market (Hutt, 2016). Considering reported labelling discrepancies of nicotine content in e-liquid products previously (Trehy et al., 2011; Kim et al., 2015; Geiss et al., 2015), thus, it is important to monitor the chemical contents of the local products as there is no local standard or guideline for its production.

The EC is known to be a new form of device which has similar function with conventional cigarette in delivering nicotine and other chemicals to its users. Therefore, the EC usage can possibly pose a health risk to the users. Referring to the previous findings, the usage of EC has been linked with various reported health effects such as increased heart rate, mouth and throat irritation and dry cough (Vakali et al., 2014; Callahan-Lyon, 2014). In this study, it would cover the estimation of non-carcinogenic health risk which resulted from the exposure to nicotine and PG, while the risk of carcinogenic health effect would be estimated due to the exposure to NNN and NNK contained in the locally-manufactured e-liquids.

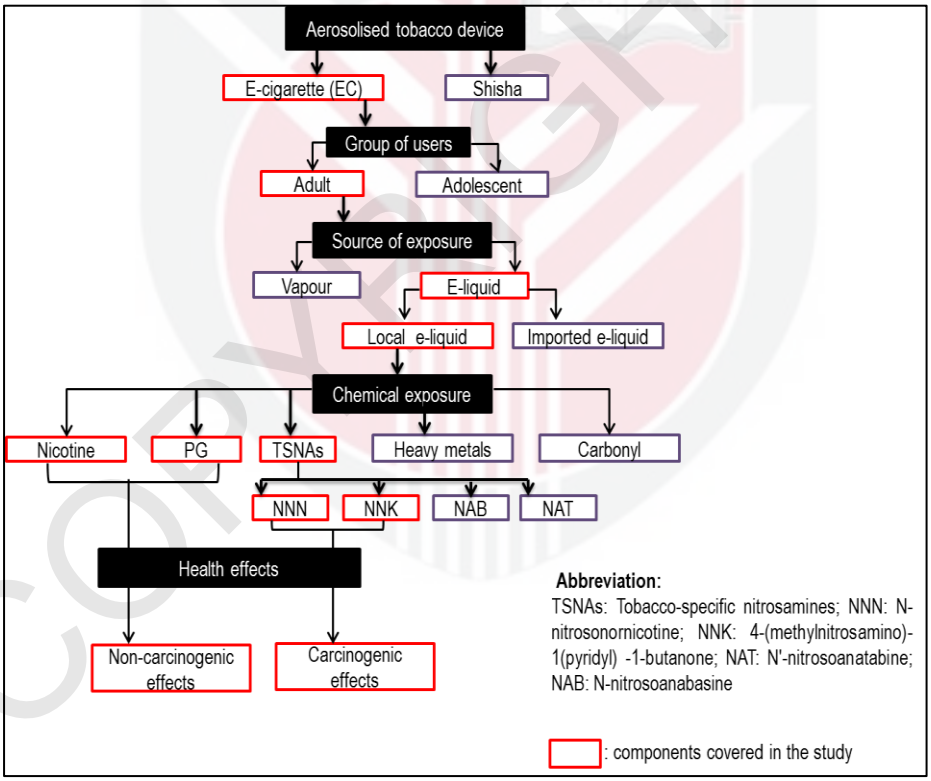


Figure 1.4: Conceptual framework of study

1.10 Flow of Study

Overall, this study is made of three elements which are linked consecutively; i) Sub-study I: Survey on EC usage; ii) Sub-study II: Chemical analysis of e-liquid samples; iii) Sub-study III: Health Risk Assessment (HRA).

In the first element (Sub-study I: survey on EC use), the community survey was conducted to gain information on EC usage topography among local EC users in the Klang Valley. In addition, this survey was also aimed to gather information from the respondents on the proportion of EC users, reasons of EC use, negative and positive views on EC, perceived effects of EC use on health symptoms, and tobacco consumption. Then, the most favoured local e-liquid products reported in this sub-study would be listed and purchased in order to be analysed for chemical contents in the sub-study II.

In the second element (Sub-study II: chemical analysis of e-liquid samples), chemical analysis of locally manufactured e-liquids was performed to determine the concentration of nicotine, PG, and TSNAs. The analysis involved local e-liquid samples that were most favoured among the respondents reported in the sub-study I.

The final output of this study was covered in sub-study III, which was the HRA. In the third element, the dose of exposure to the selected chemicals would be estimated by integrating the usage patterns data obtained in the sub-study I (such as usage duration of EC, and usage frequency) with the chemical concentrations' data generated in the sub-study II. The dose of exposure to the non-cancerous compounds (nicotine and PG) would be denoted as the average daily dose (ADD) and the lifetime average daily dose (LADD) would represent the dose of exposure to the carcinogenic compound of TSNAs (NNN and NNK). Lastly, the estimated risk would be categorised (either the exposure to the selected chemicals have potential to harm the health or otherwise) based on the value of total hazard quotient (HQ_T); which resulted from the cumulative exposure to nicotine and PG. The value of total lifetime cancer risk (LCR_T) would represent the cumulative exposure to the selected carcinogens (NNN and NNK). Figure 1.5 shows the flow of research.

1.11 Research Questions

Overall, this study consists of three sub-studies that links consecutively; i) Sub-study I: Survey on EC usage, ii) Sub-study II: Chemical analysis of the selected locally manufactured e-liquids, and iii) Sub-study III: Health risk assessment. The research questions of each sub-study are listed as following;

1.11.1 Sub-study I: Survey on EC Usage

1) What is the proportion of EC users among tobacco users in the selected populations in Klang Valley, Selangor?

2) What are the usage patterns of EC among EC users in the selected populations in Klang Valley, Selangor?
3) What are the reasons of EC use, reported effects of EC usage in terms of tobacco consumption and health symptoms, positive and negative views on EC among EC users in the selected populations in Klang Valley, Selangor?

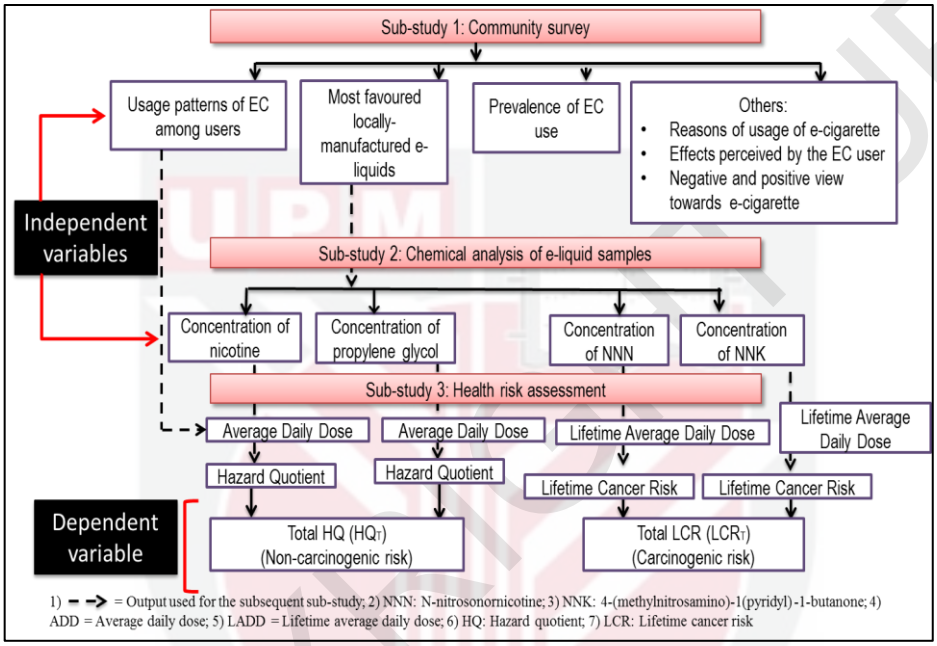


Figure 1.5: Flow of research

1.11.2 Sub-study II: Chemical Analysis of Locally-Manufactured E-Liquids

1) What are the concentrations of nicotine, PG, and selected TSNAs contained in the most favoured locally manufactured e-liquids?

1.11.3 Sub-study III: Health Risk Assessment

1) Does the exposure to nicotine and PG contained in the most favoured locally manufactured e-liquids may pose non-carcinogenic health risk to the EC users in the selected populations in Klang Valley, Selangor?
2) Does the exposure to selected TSNAs contained in the most favoured locally-manufactured e-liquids may pose carcinogenic health risk to the EC users in the selected populations in Klang Valley, Selangor?"

1.12 Definition of Terms

1.12.1 Conceptual Definitions

1.12.1.1 Conventional Cigarette

The conventional cigarette is defined as the combustible cigarette; a narrow cylinder containing tobacco and other chemicals that will produce smoke when ignited.

1.12.1.2 EC User

An EC user, or also known as a vaper, is anyone who uses an EC. EC users can be grouped into current users, ever tried users and dual users.

i) Current User

A Current user is defined as a person who has used ECs within the past 30 days (Etter & Bullen, 2014).

ii) Dual User

A dual user is defined as anyone who used EC and conventional cigarette simultaneously.

iii) Non-smoker User

An EC user never smokes a conventional cigarette before using EC.

1.12.1.3 Health Risk Assessment (HRA)

According to the United States of Environmental Protection Agency (US EPA) (2016), a human HRA is comprised of the following steps:

i) Hazard Identification

A hazard identification; the first step of HRA is defined as the process of determining whether exposure to a stressor can contribute to an increased incidence of specific adverse health effects (US EPA, 2016).

ii) Dose-response

A dose-response relationship is defined as how the amount and condition of exposure to an agent can affect or be associated with the likelihood and severity of adverse health effects (the responses) (US EPA, 2016). For non-carcinogenic, the term used is reference dose (RfD), which is defined as an estimate of the daily oral exposure of particular agent/chemical/stressor to the human population (including vulnerable subgroups), which may possibly without posing any substantial risk of detrimental health effect during a lifetime. Meanwhile, for cancer risk, the term used for the dose-response step is the cancer slope factor (CSF); an estimate of the increased cancer risk from oral exposure to a dose of 1 mg/kg-day for a lifetime (US EPA Integrated Risk Information System (IRIS), 2016).

iii) Exposure Assessment

Exposure assessment is defined as the process of estimating the magnitude, frequency, and duration of human exposure to an agent/chemical/stressor or estimating future exposures for an agent/chemical/stressor that has not yet been released (US EPA, 2016). For non-cancer effect, the average daily dose (ADD) is defined as the average doses over a period of exposure and will be considered in estimating the risk. In estimating a carcinogenic health effect risk, the lifetime average daily dose (LADD) will be taken into account. The following parameters are used in the calculation of average daily dose (ADD) for non-carcinogenic health risk, and lifetime average daily dose (LADD) for carcinogenic health risk.

a) Exposure duration (ED)

The length of time of contacts occurred between an agent/chemical/stressor and a target (the International Programme on Chemical Safety (IPCS), 2004).

b) Exposure frequency (EF)

The number of exposure events that occurred within the exposure duration (IPCS, 2004).

c) Ingestion rate (IR)

The rate at which, the medium crosses the outer exposed surface of a target during ingestion or inhalation (IPCS, 2004).

d) Averaging time (AT)

The time period which exposure was averaged (in days).

iv) Risk Characterisation

Risk characterisation is the last step of HRA, where the overall conclusion pertaining to the risk towards the agent/chemical/stressor will be concluded. This is done by integrating the information obtained from the proceeding steps of HRA; hazard identification, dose-response assessment, exposure assessment. It is defined as the risk judgment of assessor by taking into account the nature of the risk being assessed. Where the assumptions and uncertainties still existed, the further decision by a related public authority is required (US EPA, 2016).

1.12.2 Operational Definitions

1.12.2.1 Conventional Cigarette User

The operational definition of conventional cigarette user was determined using the following question: *"Do you currently smoke tobacco (conventional cigarette)?"* For those who give a response of either *"Yes, occasionally (not daily),"* or *"Yes, I smoke every day"* was categorised as conventional cigarette users.

1.12.2.2 EC User

The operational definitions for each category of EC user are as followed:

i) Current-user

In order to identify the current user of EC, the question*: "Are you currently using the electronic cigarette?"* was asked to the respondents. For those who give a response of either: *"Yes, occasionally (not daily),"* or "*Yes, I use it every day*" was categorised as current EC user.

ii) Dual user

A respondent was categorised as a dual user if they responded as follows:

a) *"Do you currently smoke tobacco (conventional cigarette)?"* by giving a response of either *"Yes, occasionally (not every day),"* or *"Yes, I smoke every day."*

b) "*Are you currently using the electronic cigarette?"* by giving a response of either *"Yes, occasionally (not daily),"* or *"Yes, I use it every day."*

iii) Non-smoker users

A respondent was categorised as non-smoker users if they responded as follows:

a) *"Do you currently smoke tobacco (conventional cigarette)?"* by giving a response of *"I never smoke a conventional cigarette."*
b) *"Are you currently using the electronic cigarette?"* by giving a response of either: *"Yes, occasionally (not daily),"* or "*Yes, I use it every day."*

1.12.2.3 Health Risk Assessment

i) Hazard Identification

In order to perform this step, literature search and reviews were systematically executed with regards to the exposure of selected chemical constituents contained in e-liquids especially nicotine, PG and selected TSNAs from the usage of EC.

ii) Dose-response

A reference dose (RfD) value was one of the parameters that was utilised in the preceding step of the HRA; exposure assessment which indicated an oral exposure to the agent. A value of 0.0008 mg/kg body weight per day of nicotine acute reference dose (RfD) had been established by the European Food Safety Authority (EFSA) (EFSA, 2009). For PG, the WHO stated that the acceptable intake of PG was 25 mg/kg (ATSDR, 1997). An average daily dose (ADD) value of population was divided by the RfD value of nicotine and PG to estimate a hazard quotient (HQ) (Equation 1.4) indicated for non-carcinogenic health risk as a result of exposure to both compounds. Considering carcinogenic health effect of NNN and NNK, the value of 1.4mg/kg/day and 1.81 x 10^{-9} µg/kg, respectively, was established by the California Environmental Protection Agency (2004) as a cancer slope factor (CSF) (mg/kg-day) $^{-1}$ value. These values were to be applied in the next step of assessment to estimate lifetime cancer risk (LCR) value as shown in Equation 1.5.

iii) Exposure Assessment

This third step of assessment was performed by assessing the data concerning the usage patterns of EC among respondent that were available and can be gathered via questionnaire. This included exposure duration (ED), exposure frequency (EF),

ingestion rate (IR), and body weight (BW). In addition, the data on the concentration of selected chemical constituents in the locally-manufactured e-liquid samples (nicotine, PG, selected TSNAs) obtained from laboratory analysis were also included with other information obtained from respondents' questionnaire to be applied in HRA further steps.

Apart from that, the further calculation was carried out using Equation 1.2 and 1.3 for this population. This was done to estimate their average daily dose (ADD) and lifetime average daily dose (LADD) respectively. The followings are the parameters used to calculate the ADD and LADD value for each respondent involved.

a) Exposure duration (ED)

Exposure duration is defined as the period of time over which respondents utilised the EC. In this study, the following question was asked to the respondents: "*In total, during your life, for how long (month) did you use the EC?"*

b) Exposure frequency (EF)

Exposure frequency is defined as the frequency of respondents' usage of EC in a week. The following question was asked to the respondents: *"Currently, on how many days per week do you use the EC?"*

c) Ingestion rate (IR)

The following question was asked to the respondents: *"On average, what was the volume of e-liquid or cartridge that you used in a month?*" Further calculation was performed to determine the intake rate, particularly, the ingestion rate of each respondent:

A millilitre of e-liquid used in a day (mL/day):

$$\frac{millilitre\ of\ e{-}liquid\ used\ per\ month}{30\ days} \qquad \text{[Equation 1.1]}$$

Average daily dose (ADD) for non-cancer risk:

$$\frac{Cp\ x\ IR\ x\ ED\ x\ EF}{BW\ x\ ATNC} \qquad \text{[Equation 1.2]}$$

Cp = Average concentration of chemical in e-liquid (mg/mL)
IR = Ingestion rate (mL/day)
Ed = Exposure duration (year)
EF = Exposure frequency (day)
BW = Body weight (kg)
ATNC = Averaging time (ED x 365days/year)

Lifetime average daily dose (LADD) for cancer risk:

$$\frac{Cp\ x\ IR\ x\ Ed\ x\ EF}{BW\ x\ ATC} \quad \text{[Equation 1.3]}$$

Cp = Average concentration of chemical in e-liquid (µg/L)
IR = Ingestion rate (L/day)
Ed = Exposure Duration (year)
EF = Exposure Frequency (day)
BW = Body weight (kg)
ATC = Averaging time (25,550 days/year)

iv) Risk Characterisation

For non-cancer risk, hazard quotient (HQ) was calculated using Equation 1.4 and the lifetime cancer risk (LCR) was calculated using Equation 1.5. In estimating the health risk of non-carcinogenic effect, HQ value for this population was interpreted according to Table 1.2, while for carcinogenic health risk, the interpretation of LCR value was based on Table 1.3.

Hazard quotient (HQ):

$$\frac{ADD\ (mg/kg/day)}{RfD\ (mg/kg/day)} \quad \text{[Equation 1.4]}$$

ADD = average daily dose (mg/kg/day)
RfD = reference dose of specific chemical (mg/kg/day)

Table 1.2: Interpretation of HQ value

HQ value	Interpretation
<1	Acceptable
>1	Unacceptable

Lifetime cancer risk (LCR):

$$LADD \times CSF \quad \text{[Equation 1.5]}$$

LADD = lifetime average daily dose (μg/kg/day)
CSF = cancer slope factor of specific chemical (μg/kg/day)

Table 1.3: Interpretation of LCR value

LCR value	Interpretation
$< 10^{-6}$	Clearly acceptable
10^{-6} to 10^{-4}	Acceptable
$> 10^{-4}$	Clearly unacceptable

1.13 Objectives

1.13.1 General Objectives

Generally, this study aimed to conduct health risk assessment associated with the usage of EC among adults in selected populations the Klang Valley, Selangor.

1.13.2 Specific Objectives

1.13.2.1 Sub-study I

1) To determine the proportion of EC users among tobacco users in the Klang Valley, Selangor.
2) To determine the usage patterns of EC among EC users in the Klang Valley, Selangor.
3) To determine the reasons of use of EC among EC users in the Klang Valley, Selangor.
4) To determine the positive and negative views on EC among users in the Klang Valley, Selangor.
5) To identify the reported effects of EC usage in terms of tobacco consumptions and health symptoms among EC users in the Klang Valley, Selangor.

1.13.2.2 Sub-study II

1) To determine the concentrations of nicotine, PG, and selected TSNAs contained in the most favoured locally-manufactured e-liquids.

1.13.2.3 Sub-study III

1) To estimate the carcinogenic and non-carcinogenic health risk associated with EC use among EC users.

1.14 Hypothesis

1) The exposure to nicotine and PG contained in selected locally-manufactured e-liquid may pose a non-carcinogenic health risk to EC users in the Klang Valley, Selangor.
2) The exposure to selected TSNAs contained in selected locally-manufactured e-liquid may pose a carcinogenic health risk to the EC users in the Klang Valley, Selangor.

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Aziemah Binti Zulkifli was born on 18th October 1989 in Kota Bharu, Kelantan. She furthered her study at the Kedah Matriculation College from 2007 until 2008. She joined Universiti Putra Malaysia (UPM) in the year 2008 for her undergraduate study in the Faculty of Medicine and Health Sciences and obtained a first degree in Bachelor of Sciences (Environmental and Occupational Health) in the year 2012. In 2015, she obtained her master degree in environmental health in the Faculty of Medicine and Health Sciences, UPM. Her project involved the assessment of secondhand smoke exposure and its impact on respiratory symptoms among school children in comprehensive (Melaka) and partial (Kedah)-smoke free states. Currently, she is pursuing her Doctor of Philosophy (Ph.D) in Environmental Health in Faculty of Medicine and Health Sciences, UPM under supervision of Assoc. Prof. Dr. Emilia Zainal Abidin (main supervisor), Assoc. Prof. Dr. Sarva Mangala Praveena, Professor Dr. Hasanah Mohd Ghazali, and Assoc. Prof. Dr. Amer Siddiq Amer Nordin, Her study involved in the determination of usage patterns, chemical analysis of locally-manufactured e-liquids and health risk assessment of electronic cigarette use among adults in the Klang Valley, Selangor. The followings are her participation and achievement in presenting the finding of her research works:

i. International Conference of Environmental and Occupational Health (ICEOH 2016) (May 2016) (Oral Presenter)
ii. Newton Smoke Free Home Workshop, Kuala Lumpur (Oral presenter) (May 2018)
iii. The 12th Asia Pacific Conference on Tobacco or Health, Bali, Indonesia (September 2018) (Oral presenter)

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