Chapter 1: Introduction

1.1 Background

Dengue is a disease caused by the mosquito-borne dengue virus. The dengue virus enters and infects a host organism through the skin through infected mosquito vector bite. This disease presents with various clinical findings that range from asymptomatic illness, dengue fever (DF), dengue hemorrhagic fever (DHF), to the often-lethal dengue shock syndrome (DSS) (World Health Organization, 2009). Since a decade ago, dengue infection has risen by 30-fold in 40 years (Olivieira, 2017). Female *Aedes* mosquitoes are particularly notorious for being infected and transmitting dengue virus to humans through blood meal. Aside from *Aedes aegypti* being the main vector of dengue, it also able to spread other diseases such as Zika fever and Chikungunya fever.

Up until now, there is no specific anti-dengue treatment or any vaccine effective enough to treat or prevent the disease spread (World Health Organization, 2012). That is why, to reduce the incidence number of arthropod-borne diseases such as dengue, it is preferable to target the vector life cycle as a cost-effective and efficient way to cut the chain of infection (Lemon et al., 2008). To combat the spread of not only dengue but also other arthropod-borne diseases, vector control using organic or inorganic insecticides is the most widely practiced means for sustainable and integrated eradication of mosquito-borne diseases (ROSE, 2001).

Although insect control is beneficial in agriculture and public health, it is also a source of both direct and indirect insecticide exposure for workers and the general population, respectively. Daily exposure of insecticides, such as through contaminated food products (Franklin & Worgan (Eds.), 2005), can be detrimental for human health. Principally, body exposure to most common insecticides often exhibit neurotoxic effects as most pesticides often works by targeting neurons (Coats, 2012; Peter & Cherian, 2000). Organophosphates is a class of the most commonly used insecticides. It works by interfering with neuronal transmission regulation, causing cholinergic overactivation that leads to neuronal death (Prahlow & Kincaid, 2013). Aside from the on-target neurotoxicity, organophosphates are also known to target other protein from other pathways if there is an exposed serine residue (Casida & Quistad, 2004; Lockridge & Schopfer, 2010; Marsillach, Costa, & Furlong, 2013). The fact that the organophosphates can exhibit wide target of toxicity makes it quite a dangerous substance.

Despite the obvious danger of neurotoxicity, there is one organophosphate that is allowed to be used for killing mosquito larvae, even in drinking and bathwater, known as temephos (World Health Organization, 2012). Temephos usage in clean water exploits the preference of the main dengue vector, *Aedes aegypti*, to breed in water (Dom, Ahmad, & Ismail, 2013). Considering the widespread use of temephos as a vector control for *Aedes aegypti* and the well-known harmful effects of organophosphates on human health, it raises the question of how temephos affects the human body in the long run.

Aside from the daily exposure, the concentration of substance also often affects the level of toxicity. Previous studies have discovered that the application of temephos to water containers once every month is considered effective as the residual larvicidal effect of temephos may persist for more than a month depending on water turnover rate and water salinity (Garelli et al., 2011; Pinheiro & Tadei, 2002). The fluctuation of temephos toxicity might be caused by the fluctuation and diminishing of temephos concentration overtime.

The temephos will be exposed to human through the use of bathwater in daily activities, mostly when taking a bath. When taking a bath, one will expose own skin to temephos treated water. The toxicity effect of temephos to human skin has not yet been analysed before. As mentioned before, organophosphates such as temephos can have a non-specific toxicity, which means that the skin might also be affected by the daily use of temephos treated water exposure, which makes human keratinocyte as this study’s main model.

1.2 Objectives

The study aims to:

1. Quantify the daily fluctuation of temephos concentration inside a bathwater container through a water cycle simulation.

2. Elucidate the effect of daily exposure of temephos towards the viability and survival of human keratinocytes *in vitro*.