

# **Electronic Nicotine Delivery Systems: Approach to Regulation in South Africa**

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## **Abstract**

### **Background**

The explosion in the popularity and use of e- cigarettes over the last decade has raised concerns and incited intense discussions over their safety, efficacy and potential public health impact. Globally there is dramatic variation in the approach to regulation, with certain jurisdictions attempting to regulate e-cigarettes either as tobacco products, medicines, consumer products or poisons whilst others have banned their use and sale. The aim of this study was to review the e-cigarette regulatory strategies adopted by the World Health Organisation, Australia, European Union and United States in an attempt to identify feasible approaches to the regulation of e-cigarettes in South Africa within the context of existing institutional regulatory frameworks.

### **Methods**

The principles of an explorative comprehensive literature-based review using a thematic qualitative approach were employed. The primary method of data collection was documentation, collected and selected using document review and analysis.

### **Results**

The strategies between jurisdictions studied vary significantly in their approach to e-cigarette regulation with each equally facing challenges and massive criticism. The South African approach to the medicalisation of e-cigarettes when evaluated against the WHO FCTC regulatory objectives was found to be ineffective and warrants a change in strategy. Within the existing medicine and tobacco product regulatory frameworks, SA has the option to regulate e-cigarettes as: (1) medicine; (2) tobacco products; or (3) an amalgam of the two approaches.

### **Conclusion**

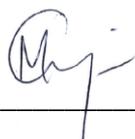
The most expeditious way for SA to regulate e-cigarettes immediately, in the absence of robust scientific data would be to implement a hybrid approach - regulation as a medicine when marketed for therapeutic use and as tobacco products when used recreationally.

**Keywords:** electronic cigarettes, e-cigarettes, electronic nicotine delivery devices, South Africa, WHO Framework Convention for Tobacco Control

## **DECLARATION**

*I declare that this thesis that I now submit for assessment on the programme of study leading to the award of Master of Science in Pharmacy Administration and Policy Regulation has not been submitted as an exercise for a degree at this or any higher education institution. It is entirely my own work and has not been taken from the work of others, save the extent that such work has been cited and acknowledged within the text of my work.*

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**Dated:** 13 November 2015

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**List of Abbreviations**

<b>ARTG</b>	<b>Australian Register of Therapeutic Goods</b>
<b>COP</b>	<b>Conference of the Parties</b>
<b>ENDS</b>	<b>Electronic Nicotine Delivery Systems</b>
<b>EC</b>	<b>European Commission</b>
<b>EMA</b>	<b>European Medicines Agency</b>
<b>EU</b>	<b>European Union</b>
<b>FCTC</b>	<b>Framework Convention for Tobacco Control</b>
<b>FDA</b>	<b>Food and Drug Administration(US)</b>
<b>FD&amp;C</b>	<b>Food, Drug and Cosmetics Act (US)</b>
<b>FSPTCA</b>	<b>Family Smoking Prevention and Tobacco Control Act (US)</b>
<b>GMP</b>	<b>Good Manufacturing Practice</b>
<b>MCC</b>	<b>Medicines Control Council</b>
<b>MOH</b>	<b>Ministry of Health</b>
<b>MS</b>	<b>Member States</b>
<b>MPD</b>	<b>Medicinal Products Directive (EU)</b>
<b>NDA</b>	<b>New Drug Application</b>
<b>OTC</b>	<b>Over the Counter</b>
<b>PMS</b>	<b>Post Market Surveillance</b>
<b>SA</b>	<b>South Africa</b>

<b>TCA</b>	<b>Tobacco Control Act (US)</b>
<b>TGA</b>	<b>Therapeutic Goods Administration (Australia)</b>
<b>TobReg</b>	<b>Tobacco Products Regulation (WHO)</b>
<b>TPCA</b>	<b>Tobacco Products Control Act (South Africa)</b>
<b>TPD</b>	<b>Tobacco Products Directive (EU)</b>
<b>US</b>	<b>United States</b>
<b>WHO</b>	<b>World Health Organization</b>



## **Glossary**

**Scheduled substance** Medicine or other substance prescribed by the Minister under section 22A. A substance can be placed in one of eight Schedules. The control over Schedule 2 to Schedule 6 substances are provided for in section 22A(5) of the Medicines Act.

**Schedule 2** In order for a substance to be listed in Schedule 2, it must be known to be substantially safe in use but require advice, counselling and management or monitoring by a pharmacist or other health professional. While medicines containing such substances may be indicated for minor disease or symptoms which can be recognised by the patient, these will require verification by a pharmacist but not an initial medical diagnosis or medical management. Schedule 2 medicines are therefore available without a prescription, but require a greater level of control than Schedule 1 medicines.

**Schedule 3** Schedule 3 medicines containing such substances can only be obtained on the prescription of an authorised prescriber. Schedule 3 substances are indicated for use in disease or conditions which require professional medical, dental or veterinary diagnoses and management.

## **Chapter One**

### **Introduction**

Electronic nicotine delivery systems (e-cigarettes; ENDS) are battery powered devices designed to deliver nicotine via inhalation by heating a solution containing nicotine, flavouring, propylene glycol and/ or vegetable glycerine (Hajek et al, 2014; Grana et al, 2014), to simulate the act of smoking without producing smoke. Initially, e-cigarettes were small devices designed to resemble traditional cigarettes. Over the last few years, they have changed significantly in product design and ingredients. Second and third generation e-cigarettes come in variety of shapes and sizes, moving away from the resemblance to cigarettes and are available in three main types: (1) disposable; (2) rechargeable with replaceable cartridges; and (3) rechargeable with a refillable tank (Grana et al, 2014).

The e-cigarette was first introduced in 2004 to the Chinese market as a smoking cessation aid (Franck et al, 2014) and extended to the European Union (EU) and United States (US) around 2006 (McRobbie et al, 2014). Its popularity and use in recent years has exponentially increased, not only among smokers who want to quit smoking, reduce their cigarette consumption (Hajek et al, 2014) or circumvent smoke-free zones, but also among smoke-naive adolescents and adults (Pepper et al, 2013). Grana et al (2014) notes that the use of e-cigarettes in the EU and the US has more than doubled among adults and adolescents from 2008 to 2012 with global sales expected to reach \$50 billion by 2030 (Hajek et al, 2014).

The sensationalism surrounding e-cigarettes has spurred feverish debate among scientists, public health experts, tobacco-control advocates, regulators, stakeholders and consumers. There are strong proponents of e-cigarettes suggesting that they aid in smoking cessation (Hajek et al, 2014) and cite them as healthier alternatives to traditional cigarettes (Saitta et al, 2014), and equally strong opponents suggesting that they perpetuate nicotine addiction (Hajek et al, 2014), endanger the long-term tobacco-control policies of deglamourising smoking and act as “gateway” products to tobacco smoking. Further concern is expressed at the paucity of scientific evidence on the long-term health effects and efficacy (Saitta et al, 2014).

Due to the uncertainties surrounding e-cigarettes – the nature of the product and the impact on public health – regulations globally are starkly contradictory. Some jurisdictions explicitly ban all sales of e-cigarettes whilst others fail to enact any legislation. Regulatory strategies

adopted include classifying e-cigarettes as tobacco, medicinal or consumer products; ENDS or poisons based on nicotine content, purpose of use and legal language (Institute for Global Tobacco Control, 2015).

The World Health Organisation (WHO), in its 2014 report produced for the Conference of the Parties (COP) to WHO Framework Convention for Tobacco Control (WHO FCTC, 2014), recommends regulatory strategies that countries can adopt to regulate ENDS. Supporters of e-cigarettes make arguments for a lighter approach to regulation, lest legislation impede the promise of e-cigarettes to reduce tobacco smoking, whilst opponents support a stricter approach until conclusive scientific evidence can support the potential harms or benefits of ENDS (Grana et al, 2013).

Currently in South Africa (SA), nicotine-containing and nicotine-free e-cigarettes fall under the ambit of the Medicines and Related Substances Control Act, 1965 (Act 101 of 1965) [herein referred to as the Medicines Act] and requires registration as a medicine prior to sale, if marketed as therapeutic products or if used as a substitute for tobacco products (Stassen, 2013; Schedules to Medicines Act, 2015). Despite the requirements for registration as a medicine, e-cigarettes with uncertain safety and quality standards are widely and freely available (Stassen, 2013b). Local sellers are circumventing the law and argue that their products fall outside the remit of the Medicine Control Council (MCC) as they make no explicit medicinal claims (Burnbridge, 2014; Twisp— ‘e-cigarettes explained’, 2015).

The quandary for regulators in SA and globally, is determining whether e-cigarettes should be banned, regulated as tobacco, medicinal products, consumer products or under a new “fit for purpose” regulatory framework, in the wake of imperfect health effects and unknown public health consequences. Determining an optimal approach to regulation that has a positive impact on public health without undermining tobacco-control policies is a certain priority. The aim of this study is to therefore identify approaches to the regulation of e-cigarettes in SA.

## **Chapter Two**

### **Literature Review**

#### **2.1 Introduction**

The global debate on the safety of e-cigarettes and their efficacy in smoking cessation is intensifying as acceptance and use of e-cigarettes radically escalates. E-cigarettes pose new challenges to regulation due to variations in definition (Feldman, 2015), their unique method of nicotine delivery, incomplete scientific data on safety and efficacy (Paradise, 2013) and the potential positive or negative influence on tobacco-control policies. The rapid advancements in technology and the lack of agreement on the public health impact of e-cigarettes equally add to the regulatory confusion and have led globally to the emergence of a dense regulatory web. Regulators in different jurisdictions pursue permissive or probationary e-cigarette regulations (Feldman, 2015), based on opinions, anecdotes, naïve optimism and pessimism, and conflicting scientific evidence. Furthermore, there is little consensus among regulators on whether e-cigarette policies should utilise pre-existing institutional regulatory frameworks or draft “fit-for-purpose” e-cigarette regulations.

The background to the WHO FCTC and the relevance thereof to e-cigarette regulation is presented in Chapter 4. It includes a review and evaluation of the policy recommendations proposed by the WHO FCTC in 2014 for ENDS regulation. Next, the scope of the current and proposed legislative provisions and regulatory frameworks as applied to e-cigarettes in Australia, the EU and US are reviewed and assessed. The limitations and key concerns of the regulatory regimes are also highlighted and discussed. In Chapter 5, the scope and limitations of the South African Medicine regulatory framework as applied to e-cigarettes is reviewed and the effectiveness evaluated against the attainment of the WHO FCTC policy objectives on ENDS proposed at the 2014 COP. The regulatory framework for tobacco products and the relevance to e-cigarettes is presented next. The chapter concludes with the proposal of strategies for e-cigarette regulation in SA, within the context of the existing Medicines Act and the TPCA. In the final chapter, concluding statements, limitations of the study and future research opportunities are presented.

## **2.2 Opinion on safety and efficacy**

As Farsalinos and Le Houezec (2015) point out, advocates and detractors tend to base their disagreements on the same characteristics and properties of e-cigarettes – resemblance to smoking and unique method of nicotine delivery. Advocates regard these as positive characteristics whilst detractors see them as negatives.

Critics express concern at the exiguity of scientific evidence on the safety and effectiveness in smoking reduction and cessation (Saitta et al, 2014). E-cigarettes are further characterised as “gateway” products to tobacco smoking, especially among “smoking naïve” adolescents and adults (Pepper et al, 2013). The potential for perpetuation of nicotine addiction also raises concern and may actually increase cigarette use (Hajek et al, 2014; Saitta et al, 2014). Survey studies conducted by Grana et al (2014); and Goniewicz and Zielinska-Danch (2012) demonstrate that use among adolescents and adults are increasing. However, reasons for the increase are unclear making it difficult to ascertain the potential as a gateway product. The lack of evidence on the ability to deliver nicotine to satisfy withdrawal effects, the potential to reverse tobacco-control policies and the effects of second-hand vapour on users and bystander are additional concerns expressed (Glynn, 2014; WHO FCTC, 2014).

Conversely, advocates cite e-cigarettes as healthier alternatives to traditional cigarettes and welcome them as a tool in harm reduction policies (Hajek et al, 2014; Saitta et al, 2014; Caponnetto, 2013a). Various safety studies have been conducted that support this argument. A systematic review by Burstyn (2014) concluded that no evidence exists to indicate that e-cigarettes produce contaminants that would warrant health concerns. However, he concedes that chronic inhalation data is insufficient. Schripp et al (2013) concluded that the effect of e-cigarette vapour on bystanders is minimal compared to traditional cigarettes.

Internet surveys show some evidence of efficacy in smoking cessation (Etter, 2010; Siegel et al, 2011). Moreover, a randomised controlled trial comparing the efficacy in smoking cessation with approved nicotine patches showed that e-cigarettes were as effective as the patches with similar adverse event profiles (Bullen et al, 2013). Similarly, pilot studies conducted by Polosa et al (2011) and Caponnetto et al (2013b) concluded that e-cigarettes may aid in smoking cessation. The authors do concede that further studies are required to unequivocally cement the association.

Farsalinos and Le Houezec (2015) sum up the debate on the review of the available evidence on e-cigarettes perfectly – “The reviews on the safety and efficacy of e-cigarettes analysing almost the same studies, results in substantially different conclusions.” The conflicting conclusions further lead to the confusion and difficulty in effecting an appropriate approach to the regulation of e-cigarettes.

### **2.3 WHO stance on e-cigarettes**

The report produced for the COP to WHO FCTC (WHO FCTC, 2014) addressed the regulatory issues pertaining to ENDS and advised a hard-line precautionary approach to regulation, suggesting a two-tiered strategy - regulating ENDS as both a tobacco product and a medicinal product, based on nicotine presence and purpose of use.

The policy recommendations were based on a review of the scientific evidence available at the time. The report concluded that the toxicity of e-cigarettes to users and non-users although lower than that of traditional cigarettes (Czogala et al, 2014), still poses some level of risk to the use of ENDS (WHO FCTC, 2014). As the level of risk reduction is unknown, WHO proposed a precautionary approach.

The report further concluded that the evidence on efficacy in smoking cessation is inconclusive and contradictory. The report did however acknowledge that evidence provided by the studies conducted by Bullen et al (2013) and Brown et al (2014) seemed promising - “the use of appropriately regulated ENDS may have a role to play in supporting attempts to quit”, but additional robust research is required (WHO FCTC, 2014).

### **2.4 Regulatory status of e-cigarettes**

#### **2.4.1 Australia**

The supply, possession and use of nicotine-containing e-cigarettes for non-therapeutic purposes are banned in Australia (Griffith, 2015; TGA ‘electronic cigarettes’, 2015). Possession or use of nicotine-containing e-cigarettes marketed for therapeutic use is also illegal unless specifically authorised and licensed by the Therapeutic Goods Administration (TGA) as a “therapeutic good”. Nicotine-free e-cigarettes are illegal in some States, dependant on State legislation passed (Douglas, 2015).

### **2.4.2 European Union**

The import, sale and use of nicotine-containing and nicotine-free e-cigarettes are currently permissible in the EU, subject to adherence to relevant legislation. Nicotine-containing e-cigarettes marketed for therapeutic or recreational use are subject to regulation under the provisions of the Tobacco Products Directive (TPD) (2014/40/EU) as a separate class of “nicotine containing products”. Conversely, nicotine-containing e-cigarettes marketed as therapeutic products are subject to regulation under the provisions of the Medicinal Products Directive (MPD) (2001/83/EC) as a “medicinal product”. Nicotine-free e-cigarettes, irrespective of health claims made, fall outside the jurisdiction of the TPD (2014/40/EU) and the MPD(2001/83/EC) and are unregulated and freely available. To date, no e-cigarette has been evaluated for safety, quality and efficacy by the European Medicines Agency (EMA) or the competent authority of any of the Member States (MS).

### **2.4.3 United States**

In the absence of Federal legislation; the import, sale, use and marketing of non-drug e-cigarettes is permitted and are widely available. Current Federal regulation exists only for nicotine-containing e-cigarettes marketed for therapeutic purposes. These products are subject to the Food and Drug Administration’s (FDA) jurisdiction over drugs and devices under the Federal Food, Drug and Cosmetic Act (FD&C Act). As of October 2015, no public announcement of any e-cigarette company submitting a drug approval application for the registration of an e-cigarette product to the FDA.

The FDA has issued a “proposed rule” to establish its active authority to regulate all products meeting the statutory definition of a “tobacco product” including non-drug e-cigarettes (FDA Proposed Rule, 2015). This is in accordance with the Federal courts’ clarification of the FDA’s authority under the FD&C Act as amended by the 2009 Family Smoking Prevention and Tobacco Control Act(TCA) (Sottera, Inc. V. FDA, 627 F.3d891 (D.C. Cir 2010)). To date, the proposed rule is still under review by the FDA and has not been finalised or adopted.

### **2.4.4 South Africa**

The legislation relevant to the regulation of e-cigarettes does not specifically address or refer to e-cigarettes. The import and sale of nicotine-containing e-cigarettes, irrespective of

therapeutic claims made is currently permissible, subject to registration as a medicine under the provisions of the Medicines Act, 1965, (Stassen, 2013b). Whereas, nicotine-free e-cigarettes marketed for non-therapeutic purposes fall outside the remit of said Act, and as such are not subject to regulation

Failure to register the e-cigarette product with the MCC prior to marketing is tantamount to contravention of Section 15 of the Medicines Act. To date, there are no registered e-cigarettes in SA and no application has been submitted to the MCC for registration (MCC SIAMED Database, 15 October 2015).

## **2.5 Summary**

Champions of e-cigarettes emphasise the potential to aid in smoking cessation, their comforting similarity to regular cigarettes, likelihood that they are considerably safer than combusted cigarettes and their absence of second hand smoke as advantages. They argue that permissive rather than prohibitive e-cigarette policies could potentially facilitate the replacement and optimistic extinction of traditional cigarettes with e-cigarettes resulting in a net benefit to public health (Feldman, 2015).

Detractors urge more caution concerning their widespread use and emphasise the lack of scientific evidence on long-term safety and efficacy as a cause for apprehension. They recommend a precautionary approach, enacting stricter flexible regulations until greater knowledge regarding the harms, benefits and impact on public health is gained (Saitta et al, 2014).

The predicament that SA and global regulators find themselves in, is attempting to formulate regulations on e-cigarettes in an environment filled with incongruous evidence on the safety, efficacy and risks to public health.

This research study aims to identify approaches to the regulation of e-cigarettes in SA, specifically in the context of existing regulatory frameworks. The knowledge sought by this research should provide a perspective on how e-cigarettes can be regulated in SA. More specifically the objectives of the study are:

1. To review and evaluate the objectives and policy recommendations made at the 2014 COP to WHO FCTC on e-cigarettes;

2. To review, evaluate and identify limitations and key concerns with the existing and deeming regulatory strategies for e-cigarettes in Australia, EU and the US;
3. To review the current legal status and regulatory framework of e-cigarettes in SA and evaluate the apparent effectiveness of the regulatory regime; and
4. To propose alternative e-cigarette regulatory strategies in the context of the existing National Tobacco and National Medicine regulatory frameworks in SA.



## **Chapter Three**

### **Methodology**

#### **3.1 Introduction**

This study employs the principles of an explorative comprehensive literature-based review using a thematic qualitative approach. The primary and only method of data collection was documentation, collected and selected using document review and analysis. The methodology chosen was in keeping with the aims and objectives of the study to propose alternative strategies.

#### **3.2 Research Approach**

The distinction between qualitative and quantitative research is a methodological issue. The decision to choose a specific methodology should be based on its suitability to answer the research questions (Bryman, 1988). Jesson et al (2011) and Lin (2009) describe a comprehensive literature-based review as “an iterative, thematic approach to research where qualitative analysis is used to classify information contained in literature and come to a conclusion on the basis of qualitative description”. Qualitative analysis has value in comparing literature, analysing and proposing alternative strategies (Jesson et al, 2011).

Document analysis is defined as a “systematic procedure for reviewing or evaluating documents” (Bowen, 2009). It requires that data be examined and interpreted in order to elicit meaning, gain understanding and develop empirical knowledge (Corbin & Strauss, 2008), by finding, selecting and appraising data contained in documents. Data is then organised into major themes and categories through content analysis (Bowen, 2009). Thematic analysis entails recognising patterns within the data, with emerging themes becoming the category for analysis (Fereday and Muir-Cochrane, 2006). Document analysis has served mostly as a complement to other research methods but it is also recognised as a stand-alone method (Bowen, 2009).

Criticism of the literature-based review method is that it is not methodological, has no clear cut design, lacks transparency of the method and cannot be duplicated (Aveyard, 2010). Additionally, the possibility of potential bias or selection bias is high (Bowen, 2009). Low retrievability of data is also raised as a disadvantage to the use of this type of research. The significant difference from other methodologies is that it does not directly deal

with the object under study but indirectly accesses information from a variety of literature (Foundations of qualitative research in education, 2011).

The aim and nature of the research does not lend itself to a systematic review with or without meta-analysis. In a quantitative study all the available research on a particular topic is sought in order to determine the effect of one variable on another, either directly or indirectly. It is a thorough and comprehensive way of interrogating literature and includes among other steps, developing a detailed search strategy with explicit inclusion and exclusion criteria, with the goal of reducing bias (Uman, 2011).

### **3.3. Rationale for chosen jurisdictions**

The study aims to review, evaluate and identify concerns with the current and proposed regulatory strategies for e-cigarettes in Australia, EU and the US, with the goal to propose possible regulatory strategies for SA. A report by the Institute for Global Tobacco Control (2015) that provides descriptions of a 123 country-level laws that regulate the sale, use, advertising, promotion, taxation and /or classification of e-cigarettes, was used as the basis for determination of inclusion or exclusion of the chosen countries into the study. As determined by the policy scan, countries classify e-cigarettes as tobacco products; medicinal products; consumer products or poisons. Other regulatory strategies – advertising; sale restrictions; taxation and outright bans are also highlighted in the report.

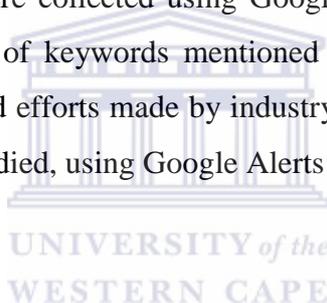
Firstly, jurisdictions that regulate e-cigarettes using one or more of the classifications above were included in the research. This yielded 48 countries; 19 regulating e-cigarettes as medicinal products, 25 countries regulating as tobacco products and 4 countries regulating e-cigarettes as poisons. European countries that form part of the EU MS were excluded as the supranational legislation of the EU is required to be transposed into National law at the MS level.

Secondly, regulatory authorities that South African regulators generally align with were then taken into consideration. This yielded three jurisdictions: US, EU and Australia (pers. Comm. MCC, 2015). Lastly, the accessibility, availability and relevance of data were also considered.

### **3.4 Data Collection**

This research method relies on primary and secondary data analysis through an extensive inquiry of legislation, regulations, policy documents, guidances, published peer-reviewed articles, books, internet based articles, newspaper articles, magazines, reports, law reviews and journals. According to Politand Hungler (2001), primary data comes from conceptual literature written by the people who developed the theory. It is first hand testimony concerning a topic under discussion. A secondary review on the other hand is a summary of the works of other authors. This study defines primary sources as legislation, regulation, guidances and other regulatory policy documents and secondary sources as published peer-reviewed articles, books, internet-based articles, newspaper articles, magazines, reports, journals and law reviews.

Data from secondary sources were collected using Google Scholar, Pubmed, Lancet, BMJ and Google inputting the string of keywords mentioned in the sub-sections below. News reports on pending legislation and efforts made by industry and public health representatives to influence the law were also studied, using Google Alerts as a mechanism to keep abreast of new developments



The collection of data is discussed below under the specific jurisdictions.

#### **3.4.1 WHO**

In order to obtain official WHO policy documents, relevant to e-cigarettes and tobacco control, the website, [www.who.int/en](http://www.who.int/en), was searched, using keywords; ‘electronic cigarettes’; ‘e-cigarettes’; ‘electronic nicotine delivery systems’; ‘ENDS’; ‘FCTC’; and ‘tobacco products’. Documents were included if they explicitly targeted e-cigarettes. Those addressing only tobacco products were excluded unless they explicitly mentioned e-cigarettes.

#### **3.4.2 Australia**

A search was performed in the TGA website and database, [www.TGA.gov.au](http://www.TGA.gov.au), to identify the official Commonwealth legislation, regulations and subordinate policy documents, using keywords: ‘electronic cigarettes’; ‘e-cigarettes’; ‘electronic nicotine delivery systems’; ‘ENDS’; and ‘Poisons’. Due to scant information retrieved, the search string was broadened

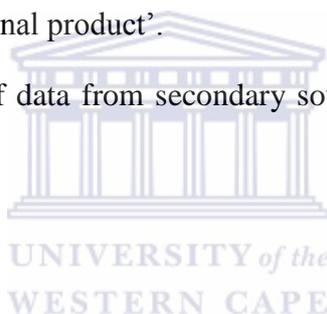
to include ‘therapeutic goods’ and ‘tobacco products’. Regulatory documents were included if they were issued at the Commonwealth level and mentioned ‘e-cigarettes’; ‘poisons’ or ‘nicotine’. Documents concerning State laws and Territory laws were included in the review only if they explicitly mentioned e-cigarettes, smoking and vaping.

The approach to the collection of data from secondary sources is as described above under Section 3.4.

### **3.4.3 European Union**

In order to obtain official EU law documents –Directive and Regulations, the databases for EUROPA and EUR-LEX were searched, using keywords; ‘electronic cigarettes’; ‘e-cigarettes’; ‘electronic nicotine delivery systems’; ‘ENDS’; and ‘tobacco products’. The EMA website was also searched, for legislation on the authorisation procedure for medicinal products using keywords; ‘medicinal product’.

The approach to the collection of data from secondary sources is as described above under Section 3.4.



### **3.4.4 United States**

A search was performed in the FDA website and database, [www.FDA.gov](http://www.FDA.gov), to identify the official Federal legislation, regulations and subordinate documents using keywords: ‘electronic cigarettes’; ‘e-cigarettes’; ‘electronic nicotine delivery systems’; ‘ENDS’; and ‘tobacco products’, specifically, enacted regulations and laws and future proposed regulations. The FDA website was also searched for information on the authorisation procedure for drugs using the keywords; ‘New drug application’.

For purposes of this review, an enacted regulation was considered an effected law whilst a proposed regulation was deemed a regulatory draft presented to the legislature for discussion and mentioned in a proposed rule by a specific agency. Regulatory documents were included if they were issued at the Federal level and explicitly targeted e-cigarettes. Documents addressing only nicotine-containing or tobacco-derived products were excluded unless they explicitly included e-cigarettes.

The approach to the collection of data from secondary sources is as described above under Section 3.4.

### **3.4.5 South Africa**

A search was performed in the MCC website , [www.mccza.com](http://www.mccza.com), to identify the official legislation, regulations and subordinate policy documents, using keywords: ‘electronic cigarettes’; ‘e-cigarettes’; ‘electronic nicotine delivery systems’; ‘ENDS’; “nicotine” and ‘tobacco products’. Due to an inefficient and ineffective search function and the lack of information on the MCC website, a further search was conducted in Google to identify the relevant legislation pertaining to medicines and tobacco products. Regulatory documents were included only if they explicitly mentioned e-cigarettes, tobacco substitutes, nicotine-containing or tobacco-derived products or nicotine.

The approach to the collection of data from secondary sources is as described above under Section 3.4.

### **3.5 Data Analysis**

In order to review and analyse the e-cigarette regulatory strategies in the various jurisdictions, data was organised into themes, and parameters for review were identified. For each jurisdiction, the following characteristics were extracted:

- ❖ Legislative system
- ❖ Definition of e-cigarette
- ❖ Strategy of regulation
  - Product class
  - Sale
  - Marketing
  - Tax/ Price
  - Use
- ❖ Regulatory Requirements
  - Pre-market requirements
  - Labelling and packaging
  - Ingredients
  - Quality and Safety Standards
  - Regulation of medicinal products/ drugs/ therapeutic goods

Where parameters were not applicable to the jurisdiction or are not covered by the regulatory strategy, these were not discussed.

### **3.6 Ethical Considerations**

No ethical issues were raised as the research is purely literature based. Ethical forms have been completed and submitted for evaluation by the relevant Ethics Committee.



## **Chapter Four**

### **Analysis and Discussion**

#### **4.1 WHO**

##### **4.1.1 Background**

The FCTC is the first international health treaty negotiated under the auspices of the WHO (WHO FCTC History, 2009). It was developed in February 2005 in response to the globalisation of the tobacco epidemic and aims to “protect present and future generations from the devastating health, social, environmental and economic consequences of tobacco consumption and exposure to tobacco smoke” (WHO FCTC Overview, 2015). As early as 2008, the FCTC addressed issues pertaining to e-cigarettes and recently made policy recommendations on the approach to e-cigarette regulation (WHO FCTC COP, 2014).

The entry of the FCTC into the e-cigarette regulation arena has stirred controversy (Oliver, 2015) as the scientific community disagrees on the applicability of the provisions to e-cigarettes. The opinion is that e-cigarettes contain only nicotine derived from tobacco or non-tobacco sources, not tobacco itself, and as such falls outside the remit of the FCTC. The FCTC has been ratified by 168 countries (WHO FCTC Parties, 2015); including South Africa (UN Treaty Collection, 2015) and many countries are taking into consideration the recommendations and reviewing the applicability to their current regulatory frameworks. The WHO’s key role in tobacco-control and FCTC gives the agency an unusual degree of moral power, although the recommendations applicable to e-cigarettes have no legal force (Feldman, 2015).

##### **4.1.2. Relevance of the FCTC to e-cigarettes**

In November 2008, the WHO Study Group on Tobacco Product Regulation (TobReg) discussed the emerging regulatory issues relevant to e-cigarettes. TobReg concluded that ENDS claiming to have health benefits, reduce harm or aid smoking cessation should be prohibited until scientifically proven and should be regulated as combination drugs and medical devices. However, if ENDS are regulated under tobacco-control laws they should be subject to the requirements in FCTC Articles 8, 9, 10, 11 and 13 (TobReg, 2009). The report articulated concerns that the sale, promotion and use of ENDS may create interference with implementation of the FCTC articles and lead to a resurgence in tobacco use. Furthermore,

the paucity of data on the safety of the ingredients in the e-cigarette solution, the safety and extent of nicotine uptake from ENDS and the lack of scientific evidence to establish smoking cessation claims, was also expressed.

The November 2012 COP to WHO FCTC report reiterated the conclusions of the 2009 TobReg report and advised a precautionary approach to ENDS regulation based on the dearth of safety studies at that time point. The report further recommended a two-pronged strategy – regulating ENDS as both a tobacco product and a medicinal product –to prevent a situation in which ENDS are available and unregulated simply because no health claims are made (WHO FCTC COP, 2012).

The 2014 COP report examined the emerging scientific evidence on ENDS; the impact on public health; and the impact on tobacco-control policies and announced a set of policy recommendations for ENDS regulation. The objectives of an ENDS regulatory strategy, as recommended by the WHO FCTC should be to: (1) prevent the uptake of ENDS by non-smokers and youth; (2) minimise potential health risks to users and non-users; (3) prevent unproven health claims; and (4) protect existing tobacco-control policies (WHO FCTC COP, 2014). The report invited parties to consider the regulatory options proposed, taking into consideration country specific frameworks and legal constraint. Lastly, the report echoes the conclusions of the FCTC COP 2012 report in recommending a hybrid strategy – “regulating ENDS as both a tobacco product and a medicinal product” – based on presentation and function.

### **4.1.3 Criticism of WHO FCTC e-cigarette policies**

The ENDS regulatory strategies proposed by the WHO FCTC has been subject to substantive peer-reviewed criticism from leading academics who found the report misleading and an inaccurate account of available evidence, calling out the WHO for using a selective approach to scientific evidence (Bates, 2014). Professor Ann McNeill from King’s College London, states: “the WHO’s approach will make it harder to bring these products to market than tobacco products, inhibit innovation and put off smokers from using e-cigarettes, putting us in danger of foregoing the public health benefits these products could have.” (McNeill, 2014)

Critics further argue that the “WHO has taken on an activist advocacy role and strayed into misrepresentation and miscommunication of the science and policy issues” (Bates, 2014). The protection of traditional cigarette sales from e-cigarette competition as an unintended consequence of over-excessive e-cigarette regulation was also articulated as a critical point of contention. The criticism is that this may potentially diminish the appeal of switching to e-cigarettes and so increase harm and cause avoidable deaths (Bates, 2014). Further, they argue that the FCTC objectives are focused exclusively on tobacco and tobacco smoke and as ENDS do not contain tobacco, the regulation thereof is incongruous and fundamentally incompatible.



## **4.2 Australia**

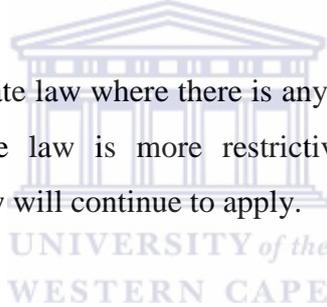
### **4.2.1 Background**

The legislation relevant to the regulation of e-cigarettes forms a complex web of Commonwealth and State law. No specific reference is made to e-cigarettes; instead, a number of laws relating to poisons, therapeutic goods and tobacco control may apply (Quit Victoria, 2015). The regulatory position differs dependant on the presence of nicotine, commercial or personal use or therapeutic versus recreational use.

### **4.2.2 Legislative System**

The legal system is three-tiered and comprises of Commonwealth, State and Territorial law (Banks, 2007). Australia is a federation of six States which have their own constitutions, parliaments, governments and laws (Quit Victoria, 2015). All of the States are separate jurisdictions and have their own system of courts and parliaments.

Commonwealth law overrides State law where there is any inconsistency between laws (Quit Victoria, 2015). Where the State law is more restrictive than but consistent with the Commonwealth law, the State law will continue to apply.



### **4.2.3 Definition**

There is currently no distinct definition of e-cigarettes; however dependant on presence of nicotine and purpose of use can fall within the statutory definitions of a “therapeutic good” or “poison”. Chapter 1, Section 3 of the Therapeutic Goods Act, 1989 (*Cth*), defines a “therapeutic good” as:

“Goods,

- a. *that are represented in any way to be, or that are, whether because of the way in which the goods are presented or for any other reason, likely to be taken to be:*
  - i. *for therapeutic use; or*
  - ii. *for use as an ingredient or component in the manufacture of therapeutic goods; or*
  - iii. *for use as a container or part of a container for goods of the kind referred to in subparagraph (i) or (ii); or .....*

The definition of a “poison” in the Therapeutic Goods Act is: “*an ingredient, compound, material or preparation which, or the use of which, may cause death, illness or injury and includes any ingredient, compound, material or preparation referred to in a schedule to the current Poisons Standard.*”

#### **4.2.4 Regulatory Strategy**

##### **4.2.4.1 Product Classification**

At the Commonwealth level, nicotine-containing e-cigarettes are classified as “poisons” or “therapeutic goods” based on the purpose of use. The Poisons Standard 2015 (Cth) lists nicotine as a Schedule 7 poison, except in preparations for human therapeutic use or in tobacco prepared and packed for smoking. It cannot be sold, supplied or possessed unless it is ‘in preparations for human therapeutic use’ or it is part of traditional cigarettes.

Nicotine for human consumption is listed in the Poisons Standard as a Schedule 4 prescription only medicine, except when used as an aid in the withdrawal from tobacco smoking in preparations intended for oromucosal or transdermal use. Non-poison nicotine-containing products must satisfy the definition of a “therapeutic good” in the Therapeutic Goods Act to be registered a medicine.

Nicotine-free e-cigarettes that purport to be of therapeutic value and are marketed as such are classified as “therapeutic goods” and subject to legislation under the Therapeutics Goods Act. Whereas nicotine-free e-cigarettes making no therapeutic claims are not covered by the laws relevant to “therapeutic goods” or “poisons” and remain unregulated.

##### **4.2.4.2 Sale**

Existing legislation in all States bans the manufacture, sale and possession of nicotine-containing e-cigarettes unless specifically licensed by the relevant authority under poison control legislation (Douglas, 2015). This is due to controls that classify nicotine as a ‘Schedule 7 –Dangerous Poison’ under the Poisons Standard (Cth) (Quit Victoria, 2015).

The import, export, manufacture and sale of nicotine-containing e-cigarettes intended for use as an aid to smoking cessation is a criminal offence under Section 9 of the Therapeutic Goods Act unless registered by the TGA as a “therapeutic good”, as is the import for commercial purposes and sale of nicotine-free e-cigarettes that are marketed with therapeutic claims.

Import and sale of nicotine-free e-cigarettes marketed as recreational products are not covered by law and are unregulated.

Import of nicotine-containing and nicotine-free e-cigarettes for personal therapeutic use is exempt from TGA registration under the personal importation scheme provided for under Schedule 5A of the *Therapeutic Goods Regulation, 1990 (Cth)*. E-cigarettes for personal therapeutic use can legally be imported into the country if all the requirements of the scheme are met.

In Western Australian the sale of nicotine-free and therapeutic claim free e-cigarettes that are similar in appearance to combustible cigarettes is an offence (Douglas, 2015). In 2014, Queensland expanded the definition of ‘smoking product’ to include ‘personal vapourisers’, so that existing laws on the prohibition of tobacco product sale to minors is applicable to e-cigarettes as well (Douglas, 2015).

#### **4.2.4.3 Marketing**

Advertising and promotion of therapeutic good e-cigarettes are subject to the provisions of the Therapeutic Goods Act (*Cth*). Tobacco control laws restricting advertising and display at retail outlets include e-cigarettes in the state of Queensland (Douglas, 2015).

#### **4.2.4.4 Taxation**

There is no Commonwealth law on excise taxation of e-cigarettes.

#### **4.2.4.5 Use**

There is no Commonwealth law regulating where e-cigarettes can be used. E-cigarettes are not directly captured under the smoke-free laws. Individual establishments and workplaces may develop their own policies in relation to the use of e-cigarettes, which may include banning their use on the premises.

Queensland applies the same restrictions on the use of e-cigarettes as those applicable to combustible cigarettes (Quit Victoria, 2014).

#### **4.2.5 Regulation of Therapeutic Goods**

Products classified as therapeutic goods are regulated under the Therapeutics Goods Act. It sets out the legal requirements for the import, export, manufacture and supply in Australia and details the requirements for listing and registering products on the Australian Register of Therapeutic Goods (ARTG), as well as advertising, labelling, and product appearance requirements.

The Therapeutic Goods Act provides a uniform national system of control over therapeutic goods (How the TGA Regulates, 2015). Other Commonwealth and State legislation may apply to certain medicines. The scheduling of substances in the Poisons Standard and the safe storage of therapeutic goods are also covered by State legislation.

TGA regulates therapeutic goods through: (1) pre-market assessment; (2) post-market monitoring and enforcement of standards; and (3) licensing of manufacturers (How the TGA Regulates, 2015). The TGA approves and regulates products based on an assessment of risks against benefits and applies scientific and clinical expertise to its decision-making to ensure that the benefits of a product outweigh any risk. The level of regulatory control increases with the level of risk the medicine can pose. The risk-benefit approach assures consumers that the products they take are safe for their intended use, while still providing access to products which are essential to their health needs.

#### **4.2.6 Limitations and Key Concerns**

The classification of nicotine as a Poison when used in products not intended for human therapeutic use or in tobacco prepared and packed for smoking, creates a *de facto* ban on nicotine-containing e-cigarettes for recreational use. Critics argue that the prohibition of the sale of a potentially less harmful way of obtaining nicotine whilst allowing the most dangerous form of nicotine delivery – combustible cigarettes – to continue to be freely available, is an unethical, illogical and incoherent form of regulation (Bates, 2014). Hall et al (2015) states: “It’s a paternalistic policy that denies adult smokers the right to use a less harmful form of nicotine”. The concern is that the ban protects the cigarette trade from e-cigarette competition, essentially curbing innovation to decrease the harms caused by cigarettes in favour of a known destructor of public health. Moreover, the sales ban leaves product quality, marketing, product information and sales to the black market (Hall et al, 2015) and prevents any sensible regulation of e-cigarettes to reduce the risks to public health.

The limitation of the regulatory ban on e-cigarettes is that it does not address the sale, possession and use of nicotine-free e-cigarettes, except in certain jurisdictions, where it is banned due to its likeness to combustible cigarettes.

Finally, the contradictions between Commonwealth and State law concerning nicotine-free e-cigarettes are concerning and causes confusion for regulators and the public, specifically the prohibition of e-cigarettes that resemble tobacco products in some States.



### **4.3 European Union**

#### **4.3.1 Background**

Prior to the revision of the TPD, e-cigarettes were regulated as general consumer products subject to chemical safety, electrical safety, weights and measures, general product and safety regulations, among others (TVECA Position Paper, 2013).

The European Commission (EC) proposed in December 2012, within the context of the TPD (2001/37/EC) revision, that all nicotine-containing products exceeding a certain level of nicotine be qualified as medicinal products and as consumer products if nicotine levels fall below the threshold (EC Proposal, 2012).

The European Council of Ministers at a June 2013 meeting adopted the EC's proposal with some amendments, notably the reduction of the nicotine threshold categorising e-cigarettes as medicinal products (Council of the European Union, 2013).

The European Parliament (EP) voted down the Commission's proposal of e-cigarette medicalisation in October 2013 and counter proposed that e-cigarettes: (1) accompanied by a therapeutic claim be regulated as medicinal products; (2) with very high nicotine levels be prohibited; and (3) other than the previous two be regulated as normal consumer products under the provisions of the TPD (EP Proposal, 2013). Agreement was reached between the 3 heads on the 18 December 2013 (EC Commissioner Borg, 2013).

The revisions of the TPD (2014/40/EU) were formally endorsed in February, adopted in April and entered into force on the 19 May 2014. The MS's have until May 2016 to transpose the provisions of the TPD into domestic legislation (Article 29(1) Directive (2014/40/EC)).

The key differences for registration of e-cigarettes as a medicinal product versus a tobacco product are discussed later on in Section 4.3.6 under the sub-heading 'Regulation of medicinal products'.

#### **4.3.2 Legislative System**

The EU is a partnership of 28 MS's working together to harmonise laws across the States (University of Oxford, 2015). The legislative system is headed by three law-making organs -

The EC; The Council of the EU; and the EP. The EC is an executive body that represents the interests of the EU as a whole and has the right of initiative to propose law for adoption by the EP and the Council of the EU. The EP passes EU law whilst The Council is the main decision making body (University of Oxford, 2015).

The binding legal instruments that make up the secondary legislation of the EU are Regulations and Directives. A Regulation has general application, is binding in its entirety and directly applicable to MS, whereas a Directive shall be binding upon each MS to which it is addressed (Moussis, 2011). Directives are formulated on a supranational level and then implemented by MS into domestic law. It defines objectives to be attained by a common policy and leaves it to MS's to choose the forms and methods necessary for complying with it. A transposition period for MS's to bring national legislation into line with the Directive is applied, failing which they are infringing European Legislation. In the case of conflict between domestic and supranational law, EU law takes precedence (Moussis, 2011).

### **4.3.3 Definition of e-cigarette**

E-cigarettes are defined as a new, non-tobacco category of products separate from tobacco products as: *“a product that can be used for consumption of nicotine-containing vapour via a mouth piece, or any component of that product, including a cartridge, tank and the device without cartridge or tank. Electronic cigarettes can be disposable or refillable by means of a refill container and a tank or rechargeable with single-use cartridge”*.

Nicotine-free e-cigarettes do not meet the TPD definition of an e-cigarette and therefore falls outside the remit of the TPD (2014/40/EC).

### **4.3.4 Regulatory Strategy**

#### **4.3.4.1 Product Classification**

The EU has adopted a “twin track” approach and opted to classify nicotine-containing e-cigarettes as consumer products regulated under the provisions of the TPD unless authorised pursuant to the MPD (2001/83/EC) as a medicinal product. The basis of the classification lies in the nicotine concentration of the product and the accompanied manufacturer claims. The maximum concentration of nicotine allowed in e-cigarettes is 20 mg/ml and the liquid must not exceed 10 ml in dedicated refill containers and 2 ml in single-use cartridges or disposable e-cigarettes (Article 20(3)(a) and Article 20(3)(b)).

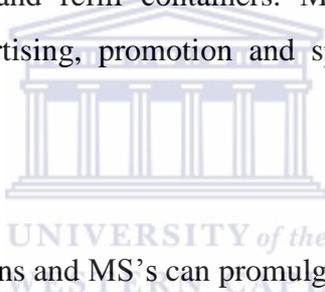
#### **4.3.4.2 Sale**

The sale of nicotine-containing e-cigarettes marketed for therapeutic and recreational use is permissible, pursuant to authorisation under the MPD and the TPD, respectively. Article 18, which makes provisions related to cross-border distance sales of tobacco products, is extended to include e-cigarettes. Cross-border distance sale is not banned at the supranational level but MS's may choose to prohibit such sale. The sale of nicotine-free e-cigarettes is unregulated by the EU and therefore freely available to sell.

As the TPD makes no provisions on the minimum age for purchase of e-cigarettes, MS's are free to regulate sale to minors within the remit of their own jurisdictions.

#### **4.3.4.3 Marketing**

Article 20(5) of the TPD restricts cross-border advertising, promotion and sponsorship of nicotine-containing e-cigarettes and refill containers. MS's can include restrictions and requirements for domestic advertising, promotion and sponsorship of e-cigarettes within domestic legislation.



#### **4.3.4.4 Taxation**

The TPD is silent on tax restrictions and MS's can promulgate their own domestic regulations on excise tax.

#### **4.3.4.5 Use**

Article 20 of the TPD makes no provisions for the use of e-cigarettes in public places and smoke-free environments. More so, the smoke-free laws under the TPD have not been extended to e-cigarettes. MS's are free to regulate where nicotine-containing and nicotine-free e-cigarettes are used.

### **4.3.5 Regulatory Requirements**

#### **4.3.5.1 Pre-market**

There is currently no requirement under the TPD for the registration of manufacturers or importers, or for pre-market approval of e-cigarettes or refill containers. A notification to the competent authorities of the relevant MS is required as provided for in Article 20(2), of any such products which they intend to place on the market, as well as a new notification for any substantial modification to a product. The notification template mandates full disclosure of

product and ingredient information, including ingredient lists, toxicological data and description of components used and the production process.

#### **4.3.5.2 Control over Ingredients**

Restrictions and prohibitions on ingredients and the maximum concentration and volume levels of nicotine permissible in e-cigarettes and refill containers are provided for in Article 20(3). Additionally, Article 7(6) which provides for the restriction on additives is extended to apply to e-cigarettes. The responsibility for the regulation of flavours in e-cigarettes is transferred to the MS as the TPD is silent on this issue.

#### **4.3.5.3 Labelling and Warnings**

General labelling and warning requirements for unit packets and secondary packaging are listed in Article 20(4)(b) and include: list of ingredients; nicotine content and delivery per dose; batch number; recommendation to keep the product out of reach of children; and health warnings.

Additional requirements to include an information leaflet are provided for in Article 20(4)(a) and include: instructions for use and storage; contra-indications; warnings for specific risk groups; adverse effects; addictiveness and toxicity; and contact details of the manufacturer or importer.

#### **4.3.5.4 Product Quality and Safety Standards**

Article 20(3)(f) requires that e-cigarettes deliver nicotine doses at consistent levels under normal conditions of use i.e. deliver the same dose at each inhalation. The requirement that only ingredients of a high purity are used in the manufacture of the nicotine-containing liquid is set out in Article 20(3)(d).

#### **4.3.5.5 Packaging**

The requirement that e-cigarettes and refill containers are child and tamper-proof; are protected against breakage and leakage; and have a mechanism that ensures refilling without leakage is provided for in Article 20(3)(g).

#### **4.3.5.6 Post- Market Surveillance**

Article 20(7) requires manufacturers and importers of e-cigarettes or refill containers to submit annually to the MS, information on: sales volumes; consumer preferences; mode of sale of the product; and summaries of any market surveys conducted.

In addition, MS's shall monitor market developments of e-cigarettes including evidence of 'gateway' addiction. Article 20(9) requires manufacturers, importers and distributors of e-cigarettes or refill containers to establish and maintain a system for collecting information on all suspected adverse effects on human health.

#### **4.3.6 Regulation of Medicinal Products**

Article 20(1) states that the TPD does not apply to nicotine-containing e- cigarettes that are subject to authorisation under the MPD (2001/83/EC). Products classified as "medicinal products" are regulated under the MPD as amended by Directive (2004/27/EC) and Regulation (EC) No 726/2004.

As per Article 1.2 of the MPD a "medicinal product" is:

*“(a) any substance or combination of substances presented for treating or preventing disease in human beings or animals.*

*“(b) any substance or combination of substances which may be used in or administered to human beings or animals with a view to making a medicinal diagnosis or to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action”.*

Under this definition, a product can be defined as a "medicinal product" according to either its presentation or function. A product is considered as such when it satisfies one of both definitions. Therefore, e-cigarettes claiming to aid in smoking cessation and smoking reduction fit the definition of a "medicinal product" and are subject to the provisions of the MPD.

The key differences for registration of e-cigarettes classified as a medicinal product versus a consumer product are:

- Medicinal products are subject to a requirement for pre-market authorisation. Products cannot be placed on the market until authorisation has been granted by the relevant competent authority of the MS or by the EMA (Article 6.1 of Directive 2001/83/EC);

- New medicinal products will only be authorised if they meet the high Safety, Quality and Efficacy standards;
- Applications for authorisation must contain a full technical dossier, containing detailed information on clinical trials, therapeutic information and side effects;
- The risk-benefit ratio must be considered favourable and therapeutic effect must be sufficiently substantiated;
- Medicinal products must be manufactured in accordance with Good Manufacturing Practice (GMP); and
- Advertising of medicinal products are allowed under certain circumstances i.e. over the counter (OTC) versus prescription (Article 88 of MPD);
- Sale of medicinal products is subject to rules limiting their sale to pharmacies, dependant on registration conditions and scheduling classifications. Restrictions may apply on where e-cigarettes can be sold i.e. General Sale versus Pharmacy Only;
- Extensive PMS is required for medicinal products; and
- Medicinal products are subject to a lengthy registration process.

#### **4.3.7 Limitations and Key Concerns**

The TPD, despite it being the most comprehensive legislative framework for e-cigarettes to date, has received substantial criticism. Clive Bates, an advocate of e-cigarettes termed the TPD “a catalogue of poorly designed, disproportionate and discriminatory measures that will achieve nothing useful but do a great deal of harm. The harmful unintended consequences are likely to far exceed any intended benefit.” (Bates, 2014)

The primary concern is that clumsy regulation would marginalise the potential benefit of e-cigarettes, make them less competitively priced compared to tobacco cigarettes and ultimately lead to a shift back to cigarette use and the renormalisation of smoking (Vranks, 2014). The faults raised echo those of the critics of the WHO FCTC policy recommendations on ENDS - that the regulatory measures are overly stringent, even more so than those applied to traditional cigarettes, counterproductive and not commensurate with the harms of e-cigarettes relative to tobacco cigarettes (Bates, 2014).

Firstly, the procedural and substantive process surrounding the adoption of the TPD by the Council of the EU is being questioned and is likely to be found in breach of key treaty

principles (Bates, 2015b). The denunciation is that the revised Directive was hastily contrived behind closed doors without any consultation (Bates, 2015b). Totally Wicked, UK's largest e-cigarette manufacturer launched a formal legal challenge, challenging the European dictat and the rationality of Article 20 at the Court of Justice of the EU in Luxembourg. The challenge is based on the view that Article 20 represents a disproportionate impediment to the free movement of goods and free provision of services, places e-cigarettes at an unjustified competitive advantage to tobacco, fails to comply with the general principle of equality and breaches the fundamental rights of e-cigarette manufacturers. Judgement is due to be passed only in early 2016 (Ross, 2014; Irish Vape Vendor Association, 2015).

Secondly, the ban on almost all marketing unintentionally protects the cigarette trade from a disruptive challenger and is unjustified, anti-competitive and disproportionate relative to tobacco (Bates, 2015b).

Thirdly, the threshold imposed on nicotine liquids and the restriction on the volume of refill containers is arbitrary and unjustified. The claim is that the concentration maximum was set using data from a study by Farsalinos et al (2014) 'Evaluation of electronic cigarette use (vaping) topography and estimation of liquid consumption', which was misinterpreted by policy makers (Cameron, 2014). Advocates suggest that the more concentrated liquids are used by heavy smokers and that a switch to the lesser concentration may lead to unsatisfactory nicotine inhalation and a possible relapse to cigarettes (Bates, 2015a).

Fourthly, the mandatory warnings required on packs and the inclusion of leaflets is incommensurate to the risk relative to traditional cigarettes. This creates a perception of equal risk and harm to the consumer and fosters unwarranted fears. More so, mandatory leafleting is regulatory overkill and will further inflate prices (Snowdon, 2015). The frustration is that there is no similar requirement for traditional cigarettes to include leaflets.

Fifthly, the requirement that e-cigarettes deliver nicotine doses at consistent levels is impractical as the strength of each intake depends on the individual i.e. nicotine per puff. The concentration of nicotine a puff of vapour could contain and the testing required to prove that delivery is consistent could cost tens of thousands of Euros per product in research and development and quality and safety assessments (Snowden, 2015; Bates, 2015a).

In addition, the notification requirement and additional compliance burdens to market an e-cigarette will place a heavy cost burden on manufacturers which will be passed on to the consumer. As a result, there will be fewer suppliers in the market, innovation will be hindered and the availability of e-cigarettes relative to combustible cigarettes will dwindle.

The criticism raised extends to the medicinal licensing requirement for e-cigarettes marketed as therapeutic products. Proponents argue that the regulatory pathway is overly stringent, burdensome and imposes numerous requirements that make sense for medicinal products, but not e-cigarettes. Consequently, the costs for e-cigarettes would increase and the accessibility would be hampered, making tobacco cigarettes a more attractive choice for smokers. Furthermore, innovation and further development will be mired, as small improvements will require new licence applications, extending the innovation timescale and dramatically increasing the cost of innovation.

Lastly, differential regulation, medicinal versus consumer, may cause price discrepancies. The well-studied, safe, effective medicinal product will always cost more, be less appealing and less available than the freely available consumer product. This could disincentivise research into the safety, quality and efficacy of smoking cessation products in favour of regulation as recreational substitutes for tobacco cigarettes (Cobbs, 2013).

## **4.4 United States**

### **4.4.1 Background**

In June 2009, Congress granted FDA the authority to regulate “tobacco products” by enacting the TCA (Lindblom, 2015) that grants FDA sweeping oversight and enforcement authority over the manufacture, sale, distribution and marketing of “tobacco products” (US FDA Centre for Tobacco Products Overview, 2015).

In the same year, the FDA attempted to regulate e-cigarettes as drug-delivery devices under the authority of the FD&C Act (Tremblay et al, 2015). In a judgement dated December 2010, the Federal Appeals Court ruled that the FDA did not have the authority to regulate e-cigarettes as drug-delivery devices under the FD&C Act unless the product was marketed for therapeutic purposes (Sottera, inc. V. FDA, (D.C. Cir 2010)). The court further ruled that e-cigarettes and other nicotine-containing products made or derived from tobacco may be considered as “tobacco products” under the TCA. Furthermore, non-drug e-cigarettes could not be regulated under FDA’s tobacco products authority unless FDA “deems” them to be “tobacco products” under the TCA (Sottera, inc. V.FDA, (D.C. Cir 2010)). The FDA assented to the court ruling in April 2011 and announced its intention to regulate e-cigarettes as “tobacco products”, (Deyton and Woodcok, 2011) and on April 25<sup>th</sup>, 2014, proposed a Federal regulation deeming e-cigarettes and other “tobacco products” to the FDA’s authority under the FD&C Act, as amended by the TCA.

Not all the provisions of the TCA will automatically apply to e-cigarettes and the FDA will have to extend the regulations to deemed products, if required. Among the regulations that do not apply are: (1) Minimum age of 18 for purchase; (2) Face-to-face sales; (3) Minimum package size; (4) Prohibition on retailer opening packages; (5) Sampling ban; (6) Allowed in adult-only facilities; (7) Characterising flavours ban; (8) Mandatory warning labels; and (9) Brand name sponsorship ban (Tobacco Control Legal Consortium, 2014).

The lack of Federal regulatory oversight has resulted in the enactment of a myriad of restrictions and regulations on the sale and use of e-cigarette by the various States. Only seven States have not enacted any regulation pertinent to e-cigarettes (Tremblay et al, 2015). According to Tremblay et al (2015), 44 states have planned or enacted 74 regulations addressing e-cigarettes, electronic smoking devices, or vapour products. The most logical,

efficient and appropriate move by the States has been to expand existing regulation aimed at combustible cigarettes to include e-cigarettes (Lindblom, 2015).

The key differences between the registrations of non-drug e-cigarettes versus e-cigarettes marketed as drugs in accordance with the FD&C Act are discussed later on in section 4.4.6 under the sub-heading 'Regulation of drugs'.

#### **4.4.2 Legislative System**

The legal system is three-tiered and is comprised of Federal, State and Local legislation. The Federal law applies to the nation as a whole and to all 50 States. The States are separate sovereigns with their own state constitutions, state governments, and state courts (Burnham, 2011). All States have a legislative branch which enacts State statutes. They retain plenary power to make laws covering anything not pre-empted by the Federal Constitution, Federal statutes, or international treaties ratified by the Federal Senate. State law can be superior to or subordinate to Federal law, dependant on the issue at hand.

The TCA preserves the authority of State governments to regulate "tobacco products" in specific respects. Since the TCA does not pre-empt State policies, the FDA's deeming regulation does not supersede existing State law. These laws will therefore continue to play a vital role in e-cigarette regulation as specified in Section 916 of the TCA.

#### **4.4.3 Definition**

At the Federal level, the deeming rule extends its authority to cover all products meeting the statutory definition of "tobacco product", as defined in Section 201(rr) of the FD&C Act (21 U.S.C 321 (rr)) as amended by the TCA as:

*"any product made or derived from tobacco that is intended for human consumption, including any component, part or accessory of a tobacco product (except for raw materials other than tobacco used in manufacturing a component part, or accessory of a tobacco product)".*

Excluded from the definition is any article that is a drug, device, or combination product as provided for in Section 201 (rr)(2) of the FD&C Act. The FDA does not intend to define e-cigarettes as a separate category as it is encompassed by the current definition of a "tobacco product". Nicotine-free e-cigarettes and e-cigarettes that use non-tobacco sources of nicotine are not covered by the definition of "tobacco products" (Lempert et al, 2014).

The absence of Federal definition for e-cigarettes coupled with the large variety of e-cigarette brands on the market using varied terminology i.e. hookah pens, vape-pens has resulted in wide variation of definitions across the States. Some States explicitly include e-cigarettes into the definition of “tobacco products” and immediately subject e-cigarettes to the same laws as conventional cigarettes without additional legislation (Lempert et al, 2014). Conversely, many States exclude e-cigarettes from the definition of “tobacco products” and opt to define them as separate categories viz. ‘vapour products’; ‘electronic cigarettes’ and ‘electronic smoking devices’ (Lempert et al, 2014), thus precluding States from regulating e-cigarettes under existing laws and regulations applicable to tobacco products.

#### **4.4.4 Regulatory Strategy**

##### **4.4.4.1 Product Classification**

The proposed regulation aims to classify non-drug nicotine-containing e-cigarettes as “tobacco products” and therefore subjects e-cigarettes to the same regulations and restrictions that the statute applies to all tobacco and tobacco-derived products under the authority of the FD&C Act (Proposed Rule, 2014). E-cigarettes, irrespective of nicotine presence marketed as therapeutic tools are already subject to registration as a drug-delivery device under Chapter V of the FD&C Act. Nicotine-free e-cigarettes marketed for recreational purposes fall outside the ambit of the FD&C Act and are currently unregulated.

##### **4.4.4.2 Sale**

Under the deeming rule, the sale of nicotine-containing e-cigarettes for recreational purposes would be permitted pursuant to the provisions of the TCA. In addition, the proposed rule extends the minimum age and identification requirements for cigarettes prohibiting the sale to minors to all products that meet the statutory definition of “tobacco product”. Section 1140.14(b)(3) of the deeming action would ban the sale of e-cigarettes in vending machines, unless the machine is located in a facility that prohibits the entrance of individuals under 18 years of age at any time. This rule would enable uniform nationwide enforcement in spite of variable State definitions of “tobacco products”.

States have the authority to enact laws concerning the sales, use and taxation of e-cigarettes. State laws to ban the sale of e-cigarettes to minors (typically under 18 years) have been enacted in at least 38 states (Tremblay et al, 2015) and in the State of Oregon, an all-inclusive sale ban was passed.

The sale of e-cigarettes, irrespective of nicotine content, marketed for therapeutic use, is prohibited unless authorised pursuant to Chapter V of the FD&C Act.

#### **4.4.4.3 Marketing**

The advertising, promotion and sponsorship restrictions that apply to “tobacco products” under the TCA do not apply to e-cigarettes under the deeming regulations. Existing regulations prohibit the distribution of free samples of any tobacco product (21 CFR § 1140.16). This provision would automatically apply to deemed “tobacco products”. Additional provisions added to the deeming regulation are the removal of non-compliant Point-of-Sale advertising that fails to conform to the new warning statement provisions.

At the State level, marketing and advertisement regulations are relatively infrequent. Constraints imposed on marketing of e-cigarettes, including television advertisement restrictions has been enacted in at least one state. Further restriction includes the requirement that e-cigarettes be stored for sale behind the counter.

#### **4.4.4.4 Taxation**

The FDA has no regulatory authority over taxation and the responsibility lies solely in the domain of the States (Tobacco Control Legal Consortium, 2015). According to Gourdet et al(2014), only the State of Minnesota explicitly applies excise taxes to e-cigarettes and two states apply excise taxation to tobacco-derived or nicotine-containing products without explicitly mentioning e-cigarettes.

#### **4.4.4.5 Use**

The FDA does not have the authority to regulate where “tobacco products” are used and as such the TCA and the deeming regulations are silent on use and smoke-free policies. States remain accountable to implement and amend smoke-free legislation and use. Some States have extended smoke-free policies that apply to “tobacco products” to explicitly include e-cigarettes whilst others have amended the definitions of “smoking” within the legislation to include vaping and e-cigarettes (Tremblay et al, 2015). States have enacted regulations that prohibit use in all smoke-free public places and in limited venues frequented by minors (Tremblay et al, 2015).

#### **4.4.5 Regulatory Requirements**

##### **4.4.5.1 Pre-Market**

Pre-market review of tobacco products unless they are ‘substantially equivalent’ to products already on the market or are found to be exempt from demonstration of substantial equivalence is required. Deemed products that were not on the market prior to February 15, 2007 would be regarded as new products and may no longer be sold until a pre-market application is submitted. Pre-market requirements include submission of but are not limited to: toxicological, behavioural, or physiologic effects of current or future tobacco products; and their constituents, ingredients, components, and additives (Section 910 FD&C Act). Annual registration of owners and manufacturing establishments is also required. Registration and product listing requirements for registered establishments is provided in Section 911.

##### **4.4.5.2 Control over Ingredients**

A listing of all product ingredients by brand and quantity must be submitted in terms of Section 904 of the FD&C Act. Furthermore, potentially harmful tobacco product constituents identified by the Secretary as harmful or potentially harmful must be submitted as well.

Federal and State laws remain silent on characterising flavours in e-cigarettes and flavour provisions have not been extended to deemed products.

##### **4.4.5.3 Labelling and Warnings**

A deemed tobacco product in package form would need to add to its label:

- the name and place of business of the manufacturer, packer, or distributor;
- quantity;
- percentage of the tobacco used; and
- the statement “sale only allowed in the United States”

Modified-risk descriptors such as “light,” “mild,” and “low,” would also need to be removed from tobacco product labelling and advertising unless the appropriate FDA order is in effect for the relevant product (Section 911 of FD&C Act.)

#### **4.4.5.4 Product Quality and Safety Standards**

Pre-market review of the deemed products will increase product consistency and oversight of the constituents would ensure quality control relative to the chemicals and their quantities being aerosolized and inhaled. At present, there is significant variability in the concentration of chemicals amongst products—including variability between labelled content and concentration and actual content and concentration

#### **4.4.5.5 Packaging**

There are no regulations at the Federal level governing restrictions and requirements on packaging. At the State level, packaging regulations have been imposed on e-cigarettes in at least one state where the requirement that e-cigarette packages be child and tamper-proof have been enacted.

#### **4.4.5.6 Post- Market Surveillance**

PMS is required for modified risk tobacco products (Section 911 of FD&C Act) to determine the impact of the modification on consumer perception; behaviour; and health, to enable the regulatory authority to review the accuracy of the determinations upon which the order was based, and to provide information regarding the use or risks of the tobacco product. The manufacturer is required to submit PMS studies annually.

The FD&C Act is silent on the PMS for new tobacco products and products currently on the market.

#### **4.4.6 Regulation of Drugs**

The definition of “tobacco product” in the TCA explicitly excludes any article that is a drug, device or combination product. Drugs are defined under Chapter V of the FD&C Act as –

*“articles intended: (1) For use in the diagnosis, cure, mitigation, treatment, or prevention of disease, or (2) to affect the structure or any function of the body”*(Section 201 (g)(1)).

The key differences in registration of non-drug e-cigarettes versus e-cigarettes regulated as drugs are:

- Drugs must receive pre-market approval by the FDA through the New Drug Application (NDA) process or conform to a "monograph" for a OTC Drug Review;

- FDA only approves a NDA after determining that the data is adequate to show the drug's quality, safety and effectiveness for its proposed use and that its benefits outweigh the risks;
- Application for authorisation must contain a full tech dossier, including detailed clinical trials, therapeutic information and side effects;
- The law requires strict adherence to GMP requirements for drugs (21CFR parts 210 and 211);
- Advertising of drugs are allowed under certain circumstances i.e. OTC versus prescription;
- Sale of drugs is subject to rules limiting their sale to pharmacies, dependant on registration conditions and scheduling classifications. Restrictions may apply on where e-cigarettes can be sold i.e. OTC versus prescription.
- Extensive PMS is required for drugs; and
- Drugs undergo a lengthy registration process.

#### **4.4.7 Limitations and Key Concerns**

Similar to the TPD, the FDA's proposed deeming rule has received considerable criticism. The primary critique is that the rule will degrade the value proposition of e-cigarettes and dissuade smokers from switching from cigarettes, thereby curbing the reduction of tobacco cigarette use or even increasing the use of cigarettes, endangering public health (Satel and Viard, 2014). The sentiment among e-cigarette supporters is that the proposed regulation is excessive, inappropriate and potentially devastating for consumers.

Firstly, the complaint is that the scientific claims made by the FDA are flawed and biased, where the FDA singles out sources with particular negative conclusions and softens overwhelmingly obvious facts about the benefits of e-cigarettes to justify the rigorous regulations (CASAA, 2014). More so, provisions are based on arbitrary claims and rationalisations rather than on the evidence.

Secondly, the pre-market requirements imposed on manufacturers would result in elimination of most small-sized companies, as the process of approval is cost prohibitive and timely. A fatal flaw in the proposed rule lies in the filing of pre-market applications. This provision applies to all products currently on the market because virtually all products were non-

existent prior to 2007. This is a potential catastrophic administrative problem that will ultimately lead to a *de-facto* ban on e-cigarettes (Satel and Viard, 2014). The additional heavy cost burden coupled with fewer suppliers on the market will take away both the prospect of innovation and the incentive to introduce new products (CASAA, 2014).

A glaring limitation of the proposed regulation is the restrictiveness of the “tobacco product” definition. Nicotine-containing e-cigarettes derived from non-tobacco sources would escape regulation under the TCA as they do not meet the prescribed definition. The same would apply to nicotine-free e-cigarettes (Lempert et al, 2014). The FDA struggled with the definitional framework of “tobacco product” within the TCA as jurisdictional boundaries were created by the legislative definition i.e. “made or derived from tobacco” (Paradise, 2013).

At the State level, tobacco-control advocates argue that exempting e-cigarettes from smoke-free policies may expose the public to simulated smoking behaviour and undermine the efforts to denormalise smoking behaviour (Lempert et al, 2014).

Lastly, the proposed rule fails to address characterising e-cigarette flavours, marketing and sponsorship of events and sale on online e-cigarettes. Opponents of e-cigarettes fear that the marketing of e-cigarettes resembles that of the tobacco industry and aims to bombard and mislead the public as to the benefits and risks. As a result, varied and hastily drafted State regulations attempt to fill the gap resulting in clumsy regulation (Feldman, 2015).

## **Chapter Five**

### **Analysis and Discussion South Africa**

#### **5.1 Introduction**

E-cigarettes are relatively new in SA but their popularity over the last five years has exponentially increased. There has been an insurgence of e-cigarette brands on the market and aggressive marketing has led to an increase in public awareness and use. Tobacco-control advocates fear that the strides made in SA to decrease tobacco smoking over the last two decades will be reversed and lead to the renormalisation of smoking. The uncertainty among opponents and supporters of e-cigarettes as to the potential benefits and/ or harms; the proliferation of e-cigarettes in the market and the legal challenge by industry calling in to question the appropriateness of the current regulatory strategy warrants a review of e-cigarette regulatory landscape.

#### **5.2 Medicine Regulatory Framework as applied to e-cigarettes**

##### **5.2.1 Background**

Prior to the revision of the Schedules to the Medicines Act to encompass e-cigarettes under the authorisations of said Act, e-cigarettes were unregulated. The MCC prompted by a referral from the South African Pharmacy Council, tobacco-control advocates and the proliferation of e-cigarettes, undertook an evaluation of e-cigarettes in 2010 (Motala&Judin, 2014). The Schedules to the Medicines Act was amended by the Minister, on the recommendation of the MCC, to expand the Schedule 3 listing of nicotine to capture nicotine-containing e-cigarettes used for smoking cessation and as tobacco substitutes, in 2012 (Schedules to the Medicines Act, 2015) (Stassen, 2013a).

##### **5.2.2 Legislative System**

SA is a constitutional democracy with three spheres of government viz. National, Provincial and Local. These three organs of state all have legislative and executive authority operating within their own delineated areas (South African Government, 2015). Parliament is the highest organ of state that can pass legislation on the National level and consists of two houses - National Assembly and National Council of Provinces. National law applies to the nation as a whole and is applicable in all nine provinces. The Medicines and Related Substances Act, 1965 (101 of 1965) and the Tobacco Products Control Act, 1993 (Act 83 of

1993) are prescribed as National legislation and can only be amended by Parliament. National law takes precedence over Provincial law, when conflict exists.

### **5.2.3 Definition**

E-cigarettes are not defined as a separate category in the Medicines Act or the regulations thereof. However, based on the presence of nicotine in the e-cigarette, irrespective of claims made and the listing of nicotine in Schedule 3 as a substitute for a tobacco product or aid to smoking cessation, falls within the statutory definition of a medicine in the said Act –

*“means any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in –*

*(a) the diagnosis, treatment, mitigation, modification or prevention of disease, abnormal physical or mental state or the symptoms thereof in man; or*

*(b) restoring, correcting or modifying any somatic or psychic or organic function in man, and includes any veterinary medicine.”*

### **5.2.4 Regulatory Strategy**

#### **5.2.4.1 Product Classification**

Nicotine-containing e-cigarettes, irrespective of purpose of use are classified as medicines, based on the presence of nicotine. Nicotine for human consumption is listed in the Schedules as a prescription only substance under Schedule 3 –

*“when intended for human medicinal use as an aid to smoking cessation or as a substitute for a tobacco product (as defined in the Tobacco Products Control Act, 1993, as amended),”* except when registered for human medicinal use as an aid to smoking cessation and presented as gums, lozenges, sprays, inhalers, or patches.

Nicotine-free e-cigarettes that purport to be of therapeutic value and make smoking cessation claims are also classified as “medicines”, based on the purpose of use. Therefore, e-cigarettes marketed as smoking cessation tools or making therapeutic claims, regardless of nicotine content, are subject to registration as a medicine under the Medicines Act. Nicotine-free e-cigarettes making no therapeutic claims are not covered by the laws relevant to medicines and are uncategorised and unregulated.

#### **5.2.4.2 Sale**

By virtue of the fact that nicotine-containing e-cigarettes are subject to registration as a medicine, the sale thereof, is prohibited without the requisite authorisation from the MCC, as prescribed in Section 14(1) of the Medicines Act. Section 22A(5) sets out the requirements for the control of the sale and supply of Schedule 2 and above medicines. As per the provisions, nicotine-containing e-cigarettes can only be sold in a pharmacy under the personal supervision of a pharmacist, on submission of a prescription from an authorised prescriber.

As nicotine-free e-cigarettes marketed for recreational use are unclassified, their sale is permitted with no restrictions on where they may be sold, who may sell them and to whom they may be sold to.

#### **5.2.4.3 Marketing**

The requirements for advertising and promotion of nicotine-containing e-cigarettes irrespective of whether therapeutic claims are made, shall comply with the advertising requirements prescribed for a medicine as set out in the Medicines Act and the regulations thereof. Section 18(2) states: *“No person shall advertise any medicine or Scheduled substance for sale unless such advertisement complies with the prescribed requirements.”*

Regulation 45(2) of the Medicines Act bans the advertisement of medicines containing a substance in Schedule 2 and above to the public. Prescribed requirements for advertisements of medicines are set out in Regulation 45(3), 45(4), 45(5) and 45(6) to the Medicines Act.

Sampling of medicines and therefore Schedule 3 nicotine-containing medicines is prohibited as prescribed for in Section 18B of the Medicines Act. Provisions for publication or distribution of false advertisements concerning medicines are provided for in Section 20 of the Medicines Act.

As nicotine-free e-cigarettes are unclassified, advertising restrictions do not apply.

#### **5.2.4.4 Taxation**

There is no current regulation on excise taxation of e-cigarettes.

#### **5.2.4.5 Use**

There is no current regulation on where e-cigarettes can be used. Smoke-free tobacco policies do not apply to the use of e-cigarettes, as they do not fit the definition of a tobacco product (Tobacco Products Control Act, 1993 (Act 83 of 1993). The extension of tobacco-free company policies in public spaces like malls and restaurants will be left up to the discretion of the owner (Innes, 2015).

#### **5.2.5 Regulatory Requirements**

Section 15(1) of the Medicines Act and Regulation 22(3) set out the requirements for the registration of a medicine in SA, in particular Section 22(3)(e): the requirement for data on the S,Q,E of the medicine. Guidelines specifying the in depth requirements for registration are also available.

#### **5.2.6 Limitations and Key Concerns**

There are no e-cigarettes registered as medicines in SA and no application has been submitted to the MCC for registration (MCC SAIMED Database, 15 October 2015). Yet, these unregistered and unapproved products with questionable safety and quality are widely available and freely accessible to the public at mall kiosks, service stations and general stores (Stassen, 2013a).

The ambiguity of the legislation and the contrasting interpretations of the Schedules by industry and regulators are cited as reasons for the proliferation of illegal e-cigarettes on the market. Industry interprets the inscription to the Schedule 3 listing of nicotine as: Nicotine is deemed a Schedule 3 substance when: “(1) intended for human medicinal use as an aid to smoking cessation; or (2) intended for human medicinal use as a substitute for a tobacco product.” They claim that their products are not intended for medicinal use and argue that they are marketed for recreational use and as alternatives to traditional smoking (Burbidge, 2014; Twisp – ‘e-cigarettes explained’, 2015). Thereby, according to their understanding, nicotine-containing e-cigarettes are not subject to registration as a medicine as they do not lay claim to aid in smoking cessation.

This interpretation is in complete contrast to the MCC intention of the inscription, which is: Nicotine is deemed a Schedule 3 substance when: “(1) intended for human medicinal use as an aid to smoking cessation; or (2) used as a substitute for a tobacco product.” Under this

clarification, e-cigarettes marketed as a substitute for a tobacco product or smoking is deemed a Schedule 3 product, irrespective of whether or not therapeutic claims are made (Stassen, 2013b).

Further to the abstruseness of the legislation, enforcement against manufacturers and importers of illegal e-cigarettes has been virtually non-existent. The Department of Health and the MCC attribute a lack of resources and capacity constraints as reasons to the lax enforcement (Quick Drink Co, *Pty. V. MCC and others*, Gauteng High Court 2014). No penalties have been imposed, thereby allowing e-cigarettes to freely enter and flood the market. The MCC in 2014 attempted to enforce the provisions of the Medicines Act and detained a consignment of imported e-cigarettes, on the basis that they were not registered as medicines with the MCC. The company, Quick Drink, lodged an interdict with the Gauteng High Court to prevent the MCC from classifying their products as medicines and enforcing the provisions of the Medicines Act against the company. The challenge cited selective enforcement of the provisions of the said Act against the company (Quick Drink Co, *Pty. V. MCC and others*, 2014).

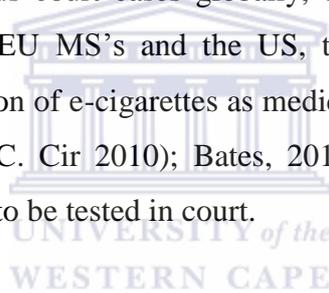
In 2015, the court granted an order against the MCC and ruled in favour of the applicant, ordering the immediate release of the seized products, citing that the MCC acted in a discriminatory manner toward the company as there are many importers, manufacturers, wholesalers and distributors in the South African market (Quick Drink Co, *Pty. V. MCC and others*, 2014). The court did not rule on the applicability of the provisions of the Medicines Act to e-cigarettes, and made a determination that a ruling is not applicable to the case (Quick Drink Co, *Pty. V. MCC and others*, 2014).

Furthermore, local e-cigarette advocates question the appropriateness and relevance of regulating e-cigarettes as medicines (Health24, 2015). The Medicines Act is seen as overly strict and cumbersome when applied to e-cigarettes (Sweanor&Yach, 2013), as it requires pharmaceutical grade manufacturing and process controls, robust scientific evidence of safety, quality and efficacy and imposes other numerous pre-market and post-market requirements. They argue that the stringency of the regulation is not commensurate with the level of risk that e-cigarettes pose. Having to go to a doctor for a prescription to quit smoking is a major barrier –cost and otherwise - to many smokers (Vegter, 2014) and leads to a situation where the more harmful product - tobacco cigarettes - is more widely available and

less regulated than the potentially safer alternative. This argument echoes the sentiments of e-cigarette advocates in the US, EU and Australia that the over-regulation of e-cigarettes could lead to an absurd situation in which e-cigarettes are treated more harshly than tobacco products. The potential of shifting use through extreme regulation from a likely healthier alternative back to combustible cigarettes is great (Oliver, 2015) and threatens to renormalise smoking behaviour more so than the use of e-cigarettes.

Globally, opponents to the medicalisation of e-cigarettes argue that regulating e-cigarettes as medicines limits further development and extends the innovation timescale, as small improvements require new applications. Consequently, the costs for e-cigarettes would increase, and cigarettes would remain a more attractive option for smokers because they are not subject to such stringent regulation.

Lastly, there have been numerous court cases globally, challenging the clarification of e-cigarettes as medicines. In the EU MS's and the US, the courts have ruled against the regulators to prohibit the regulation of e-cigarettes as medicines unless therapeutic claims are made (Sottera,inc. V. FDA, (D.C. Cir 2010); Bates, 2013). The applicability of the SA legislation to e-cigarettes has yet to be tested in court.



### **5.2.7 Effectiveness of Medicine Regulatory Strategy**

The effectiveness of the current e-cigarette regulatory regime was evaluated against the attainment of the four regulatory objectives as proposed by the WHO FCTC on ENDS.

a. Impede ENDS promotion to and uptake by non-smokers, pregnant women and youth

E-cigarettes are promoted and advertised broadly without appropriate health warnings or legal age restrictions to all persons via all communication channels in spite of the fact that the Medicines Act and the Regulations thereto restrict the advertising of Schedule 3 substances to the public. Reasons for the complete disregard of the provisions of the legislation have been outlined earlier in the chapter. The current strategy thus fails to restrict the nationwide promotion of e-cigarettes to smokers and non-smokers alike. There is no data on the uptake of e-cigarettes by users and non-users and so evaluation of evidence could not be undertaken.

b. Minimise potential health risks to ENDS users and non-users

The lack of enforcement of the provisions of the Medicines Act has led to e-cigarettes manufactured without regulatory oversight or quality, safety and efficacy standards, flooding the market and readily available. The products have not been evaluated or approved by the MCC, and the risk-benefit ratio is unknown as studies conducted to determine the impact on the potential health risk to ENDS users and non-users are inconclusive and incongruent. While there are significant restrictions on the use of tobacco in public places, where non-users might be exposed to “second-hand” smoke, no such restriction exists for e-cigarettes and the effects of second-hand vapour.

c. Prohibit unproven health claims

Only e-cigarettes approved as medicines by the MCC are permitted to make therapeutic claims. Due to the absence of enforcement, all e-cigarettes are widely available and some claim or purport to aid in smoking cessation and smoking reduction. Additional claims of improved safety over traditional cigarettes are also made. Therefore, the current regulatory strategy to regulate e-cigarettes as medicine, fails to restrict unproven health claims.

d. Protect tobacco-control efforts from other vested interest of the tobacco industry.

There is no public information on tobacco industries having stakes in e-cigarette companies in SA.

### **5.3 Tobacco Products Regulatory Framework**

#### **5.3.1 Introduction and Background**

Tobacco products are subject to regulation under the provisions of the Tobacco Products Control Act (TPCA), 1993 (Act 83 of 1993) and amendments and regulations thereof. The TPCA aims to prohibit and restrict smoking in public places, regulate sale and advertising of tobacco products and to prescribe package requirements and health warnings. The tobacco-control strategy employed by the South African government is based on two pillars – excise taxes and comprehensive legislation.

The control policies implemented have succeeded in reducing smoking prevalence among adults in SA from 35% in 2005 to 16 % in 2012 (Stassen, 2013). Over the last 2 decades, the TPCA has been amended to align the Act with the provisions of the FCTC, to include: (1) mandatory health warnings on packs; (2) prohibition of smoking on public transportation; (3) advertisement bans; (4) restriction on sale to minors; (5) restrictions on use in public places; (6) restriction of sponsorships and promotions; (7) increase of legal age to 18 years; and (8) mandatory health warnings at point of sale.

#### **5.3.2 Relevance to e-cigarettes**

The current definition of a “tobacco product” in the TPCA reads:

*“a product containing tobacco that is intended for human consumption, and includes, but is not limited to, any device, pipe, water pipe, papers, tubes, filters, portion pouches or similar objects manufactured for use in the consumption of a tobacco product”.*

The definition is restrictive to only tobacco products. As e-cigarettes do not contain tobacco, but contain nicotine derived from tobacco and non-tobacco sources, they fall outside the parameters of the current definition. As such, the provisions of the TPCA are not applicable to e-cigarettes.

Additionally the definition of “smoke” and “smoking” in the TPCA excludes vaping, vapour and e-cigarettes. As a result, mandatory smoke-free policies are not applicable to e-cigarettes, allowing their legal use in all smoke-free public places. The definition reads:

*“means to inhale, exhale, hold or otherwise have control over an ignited tobacco product, weed or plant, and ‘smoked’ and ‘smoking’ have corresponding meanings”.*

#### **5.4 Proposed Regulatory Strategies**

Various strategies to e-cigarette regulation have been identified in this study including classifying them as tobacco products, consumer products, pharmaceuticals, poisons, a combination thereof or explicitly prohibiting their sale and use. The limitations and key concerns of each strategy were presented in Chapter 4.

The favoured proposal from the COP to the WHO FCTC is the regulation of e-cigarettes as tobacco products in accordance with the FCTC provisions, unless subject to registration as a medicine when marketed for therapeutic use (WHO FCTC, 2014). Both the EU and the US regulate or propose to regulate e-cigarettes as tobacco products and medicines, but using different approaches. The fundamental difference – EU has incorporated a separate Article within the TPD that speaks to e-cigarettes with different requirements compared to tobacco cigarettes whereas in the US, the definition of tobacco products will encompass e-cigarettes and be subject to most of the regulations as that of tobacco products under the TCA.

Within the existing medicine and tobacco product regulatory frameworks, SA has the option to regulate e-cigarettes as: (1) medicines only - irrespective of purpose of use; (2) tobacco products only – irrespective of purpose of use; or (3) an amalgam of the two approaches. The limitations and key concerns with regulating nicotine-containing e-cigarettes as a medicine, for recreational or therapeutic purposes have been outlined previously in this Chapter. Regulating e-cigarettes as tobacco products only, irrespective of purpose of use, is equally inappropriate as it creates an unfair environment where nicotine-containing products claiming smoking cessation i.e. nicotine patches, inhalers and gum; will be subject to rigorous regulation as medicines whereas, e-cigarettes claiming the same would be less stringently regulated as tobacco products.

The most straightforward and expeditious way to regulate e-cigarettes, in the absence of robust scientific data would be to implement a hybrid approach - regulation as a medicine when marketed for therapeutic use regardless of the presence of nicotine and regulation as tobacco products when marketed for recreational use.

As mentioned previously, the TPCA does not make provision for regulatory oversight of e-cigarettes as the definition of “tobacco product” does not encapsulate these products and there is no explicit definition of e-cigarettes. There are three avenues available to extend the

authority of the TPCA to regulate e-cigarettes: (1) broaden the definition of a “tobacco product” to include products derived from tobacco similar to the FDA definition; (2) define e-cigarettes as a stand-alone category of tobacco products in the same vein as the EU; or (3) broaden the definition of a “tobacco product” to include products derived from tobacco and non-tobacco sources.

The advantage of the first option is that e-cigarettes that contain nicotine derived from tobacco will immediately fall under the authorisation of the TPCA, subject to all its provisions, without additional amendments to the legislation. The limitation is that e-cigarettes containing nicotine derived from non-tobacco sources and nicotine-free e-cigarettes will be excluded from the definition and will ultimately escape regulation under the TPCA.

The upside of defining e-cigarettes as a separate category is that it captures nicotine-containing e-cigarettes derived from tobacco and non-tobacco sources. The limitations are two-fold: (1) tobacco product provisions will not apply to e-cigarettes unless explicitly included in each provision or separate requirements are provided; and (2) nicotine-free e-cigarettes will escape regulation as the definition explicitly mentions nicotine.

Expansion of the “tobacco product” definition to include nicotine derived from tobacco and non-tobacco sources opens up the definition to allow for applicability to a myriad of current and future ever-evolving products. To further allow for broader applicability, the definition of “smoke” and “smoking” should be broadened to include e-cigarettes and vaping. This ensures that smoke-free laws apply to e-cigarettes irrespective of whether the product contains nicotine.

Inclusion of e-cigarettes and vaping in the TPCA immediately subjects these products to the provisions of the Act. Under the TPCA, the following provisions will apply to e-cigarettes:

- (1) Restriction of use in public places;
- (2) Restriction on advertising, promotion, sponsorship;
- (3) Prohibition on misleading information on packaging and labelling;
- (4) Requirements on packaging and labelling;
- (5) Requirements of retail display notices;
- (6) Standards for manufacturing, importing, exporting;
- (7) Prohibition of sale to minors;

- (8) Prohibition on sale of confectionary or toys that looks like or purports to represent a tobacco product;
- (9) Prohibition on internet and postal sales;
- (10) Prohibition on free distribution and bonusing;
- (11) Restriction on vending machine placement;

Additionally, the Schedules to the Medicines Act will have to be amended to clarify the nicotine inscription in Schedule 3. The portion of the inscription that makes reference to nicotine when intended as a substitute for a tobacco product should be deleted and an exception included for nicotine-containing non-medicinal products that fall under the ambit of the TPCA.

Implementing a two-pronged e-cigarette regulatory strategy would accomplish to a certain extent the regulatory objectives as proposed by the WHO FCTC. It would bar smoking cessation and reduction claims for e-cigarettes unless evaluated and approved by the MCC as a medicine. It would also end the current situation whereby nicotine-containing e-cigarettes for recreational use are subject to a much stricter regulatory regime than traditional cigarettes thereby ensuring continued product innovation and affordability, which are adversely affected when products are regulated as medicines. It would also minimise potential e-cigarette harms and maximise public health potential. Lastly, it would help safeguard critical tobacco-control gains by subjecting e-cigarettes to similar controls as tobacco products.

Although many advocates of e-cigarettes disapprove of a medicine - tobacco product strategy to regulate e-cigarettes and call for a regulatory approach specific to e-cigarettes, the uncertain and incongruous scientific evidence on these products to date warrants a precautionary approach until more studies are conducted and more evidence is gathered. A 'better safe than sorry' approach is favoured over an unregulated and unrestricted environment.

## **Chapter Six**

### **Conclusion**

This study aimed to provide perspective on how e-cigarettes can be regulated in SA now, within the existing institutional medicine and tobacco products regulatory frameworks to minimise its potential harms and maximise its potential benefits. To that end, the strategies presented and proposed provides ways that e-cigarettes will immediately be regulated and subject to the provisions of both the Medicines Act and the Tobacco Products Control Act dependant on purpose of use, even in the absence of complete scientific and behavioural data.

Between the many knowns and unknowns of e-cigarettes, there is one certainty: regulation is a necessity. However, the formulation of rational policies is challenging in the wake of limited and inconsistent scientific and behavioural evidence. Ideally, legislation should be based on a balanced risk benefit assessment at an individual and population level. In the absence of such, a precautionary approach taking into account the potential impact on public health must be considered.



### **Limitations**

The limitation of the study that must be acknowledged was that the evaluation of proposed e-cigarette regulatory strategies for SA was limited to the scope of the existing National Tobacco product regulatory framework and the National Medicines regulatory framework.

### **Future Work**

It would be of value to evaluate the feasibility of a fit-for-purpose regulatory framework for e-cigarettes that takes into account the uniqueness of the product and the differences from medicines and tobacco products.

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## **APPENDIX I**

### **Research Proposal**

#### **Title**

Electronic nicotine delivery systems: Approach to regulation in South Africa

#### **Introduction**

Electronic nicotine delivery systems (also referred to as e-cigarettes; ENDS) are battery powered devices designed to deliver nicotine via inhalation by heating a solution containing nicotine, flavouring, propylene glycol and/ or vegetable glycerine (Hajek et al, 2014), to simulate the act of smoking without producing smoke.

The e-cigarette was introduced to the Chinese market in 2004 as a smoking cessation aid (Franck et al, 2014) and in the European Union and United States around 2006 (McRobbie et al, 2014). Its popularity and use in recent years has skyrocketed among smokers who want to quit smoking, those who want to reduce their cigarette consumption (Hajek et al, 2014) and those who want to circumvent smokefree zones (Lindblom, 2015). Grana et al (2014) notes that use of e-cigarettes in the EU, US and North Korea has more than doubled among adults and adolescents from 2008 to 2012 with global sales expected to reach \$50 billion by 2030 (Hajek et al, 2014).

The sensationalism surrounding e-cigarettes has spurred feverish debate between public health experts, tobacco control advocates, regulators and industry, relating to the safety, quality, efficacy and potential public health impact. Detractors of e-cigarettes express concern at the paucity of scientific evidence on the long term health effects and efficacy in smoking cessation or harm reduction (Saitta et al, 2014) and further characterise e-cigarettes as “gateway” products to tobacco smoking, especially among “smoking naïve” youth (Pepper et al, 2013). The potential for perpetuation of nicotine addiction also raises concern as illustrated by Hajek et al (2014) and may actually increase cigarette use thereby undermining tobacco control policies. Conversely, advocates cite that they are healthier alternatives to traditional cigarettes (Saitta et al, 2014) and welcome ENDS as an alternative tool to the reduction of tobacco smoking (Hajek et al, 2014). Moreover internet surveys and clinical trials show some evidence of efficacy in smoking cessation, though some experts concede that additional studies are required.

Due to uncertainties surrounding e-cigarettes, there is dramatic variation in the approach to regulation worldwide. Certain jurisdictions explicitly ban all sales of e-cigarettes whilst others are silent on the regulation. Alternative strategies include either classifying e-cigarettes as tobacco, medicinal or consumer products; ENDS or poisons based on nicotine content, purpose of use, device components and legal language (Institute for Global Tobacco Control, 2014).

The WHO report on ENDS (Framework Convention for Tobacco Control, 2014) recommends stringent regulatory strategies, objectives and policy options that countries can adopt relative to existing frameworks and legal exigencies. Lindblom (2015) makes arguments for a lighter approach to regulation, lest legislation impede the promise of e-cigarettes to reduce tobacco smoking, whilst others support a stricter approach until conclusive scientific evidence is gathered on the harms or benefits of ENDS (Grana et al, 2013).

Currently in South Africa (SA), e-cigarettes fall under the ambit of the Medicines and Related Substances Control Act, 1965 (Act 101 of 1965) and requires registration as a medicine prior to sale. The current regime has been in place since 2012, when the Schedules to Act 101 were amended. However, inadequate enforcement of the legislation and confusion with the interpretation of the Schedules has sparked debate and is the subject of an on-going court case. According to the Medicines Control Council, all e-cigarettes are scheduled devices that require medicine registration and can only be accessed via a pharmacy on a doctor's prescription. Some experts and industry argue that only e-cigarettes claiming smoking cessation benefits require registration as medicines and other products are deemed recreational in nature.

As a result of laidback enforcement and regulatory gaps, unregistered e-cigarettes, with uncertain safety and quality, are being sold in mall kiosks, garages and general stores. Local sellers have circumvented the law by making no explicit claims that their products are medicinal, have health benefits, or aid in smoking cessation.

The quandary for regulators is determining whether e-cigarettes should be banned or regulated as tobacco or medicinal products in the wake of imperfect health effects and efficacy data and unknown public health consequences. Determining an optimal approach to regulation that has a positive impact on public health without undermining tobacco control policies is a certain priority.

In an attempt to identify feasible approaches to e-cigarette regulation in SA, the recommended strategies of the WHO and the existing and deemed regulatory strategies of the EU and US will be reviewed and critically evaluated.

In summary, this research study aims to identify feasible approaches to the regulation of e-cigarettes in SA. More specifically the objectives of the study are:

1. To present the current legal status of e-cigarettes in SA and evaluate the effectiveness of the existing framework.
2. To review and critically evaluate the WHO FCTC regulatory strategies, objectives and recommendations for e-cigarettes.
3. To provide a comprehensive review, critically evaluate and identify current concerns with the existing and deemed regulatory strategies for e-cigarettes in the EU and US.
4. To evaluate alternative e-cigarette regulatory strategies in the context of the existing national tobacco and medicine regulatory frameworks in SA.

### **Methodology**

The proposed research design is an explorative comprehensive critical literature based review using a qualitative approach. The research instrument proposed for data collection is document review. Information on e-cigarettes will be sourced from policy documents, regulations and guidances, published peer review articles, grey literature, internet based articles, newspaper articles and any other credible information sources.

Comprehensive literature review is described as an iterative, thematic approach to research where qualitative analysis is used to classify information contained in literature and come to a conclusion on the basis of qualitative description (Jesson et al, 2011; Lin, 2009). Qualitative analysis has value in comparing literature, analysing and proposing alternative strategies. The significant difference from other methodologies is that it does not directly deal with the object under study but to indirectly access information from a variety of literatures (Foundations of qualitative research in education, No date).

The criticism of the traditional literature based review is that it is not methodological, not based on a specific method, has no clear cut design, lacks transparency of the method and cannot be duplicated (Aveyard, 2010).

A systematic review using quantitative analysis is not proposed for this study due to the nature of the research. In a quantitative study all the available research on a particular topic is sought in order to determine the effect of one variable on another, either directly or indirectly.

### **Ethical Considerations**

No ethical issues are anticipated in this research as it is purely literature based. Ethical forms have been completed and submitted with this proposal for evaluation by the relevant Ethics Committee.



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