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WHO study group on tobacco product regulation

Report on the scientific basis of tobacco product regulation: tenth report of a WHO study group

World Health Organization

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Report on the scientific basis of tobacco product regulation:
tenth report of a WHO study group

World Health Organization

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Contents

Participants in the tenth meeting of the WHO Study Group on Tobacco Product Regulation xi

Acknowledgements xiv

Abbreviations and acronyms xvi

1. Introduction 1

2. Regulation of tobacco and related products. Priorities for the protection of children and young people 6

Abstract 8
2.1 Background 9
2.1.1 Introduction 9
2.1.2 WHO resources on prioritizing protection of children and young people 9
2.1.2.1 World No Tobacco Day (WNTD) 9
2.1.2.2 Nicotine- and tobacco-free schools: Policy development and implementation toolkit 9
2.1.2.3 Decisions of the COP to the WHO FCTC 10
2.1.2.4 WHO call to action 10
2.1.2.5 United Nations Convention on the Rights of the Child 10
2.1.3 Scope and aim of the paper 11
2.2 Methods 12
2.3 Prevalence and determinants of TRP use by CYA 12
2.3.1 Prevalence of TRP use by CYA 12
2.3.1.1 Overall use of one or more TRP 14
2.3.1.2 Cigarettes 14
2.3.1.3 Hookah or waterpipe tobacco 15
2.3.1.4. Cigars and cigarillos 15
2.3.1.5 HTP 15
2.3.1.6 E-cigarettes 15
2.3.1.7 Smokeless tobacco products 16
2.3.1.8 Nicotine pouches 16
2.3.1.9 Other nicotine products 17
2.3.1.10 Combined use of two or more TRP 17
2.3.1.11 Differences in TRP use by demographic and other dimensions of diversity 18
2.3.2 Factors that drive TRP use and appeal among CYA 18
2.3.2.1 Flavours 18
2.3.2.2 Non-flavour additives or other modifications that increase sensory appeal 20
2.3.2.3 Design for discreet use and concealability 20
2.3.2.4 Convenience and low cost 21
2.3.2.5 Product design that attracts CYA by resembling CYA-oriented products (including food and toys) 21
2.3.2.6 Unique CYA appeal of nicotine products, synthesized nicotine and nicotine analogue products 21
2.3.3 Abuse liability of tobacco and related products 22
2.3.3.1 Nicotine concentration 23

2.3.3.2 Method of administration 23
2.3.3.3 Additives and manufacturing processes that change pH or enhance nicotine absorption 23
2.3.3.4 Flavours and other sensory enhancers 24
2.3.3.5 Nicotine analogues and other non-nicotine psychoactive compounds 24
2.3.3.6 Device power 24
2.3.4 Impact of TRP marketing on use by CYA 25
2.4 Prioritization of protection of children and young people 26
2.4.1 Tools 26
2.4.2 Surveillance 27
2.4.2.1 Surveys 27
2.4.2.2 Observations and sales in "brick-and-mortar" stores 27
2.4.2.3 Surveillance of retailers on the Internet 28
2.4.2.4 CYA advocates and advisory groups 28
2.4.2.5 Surveillance of social media 28
2.4.3 Regulation of TRP to protect CYA 29
2.4.3.1 Overview and regulatory mechanisms 29
2.4.3.2 Comprehensive ban on manufacture and sale to CYA of all TRP or all TRP in a specific product class 30
2.4.3.3 Minimum age purchase laws 31
2.4.3.4 Restrictions on sales to CYA of TRP with specific product characteristics or design features that attract CYA 31
2.4.3.5 Marketing, packaging and advertising of TRP 34
2.4.3.6 Sales and pricing policies to limit access and affordability for CYA 35
2.4.3.7 Warning label requirements 36
2.4.3.8 Banning use of TRP in public settings 36
2.4.4 Country case studies 37
2.4.4.1 Cigarettes in Australia 37
2.4.4.2 E-cigarettes in the USA 37
2.4.4.3 E-cigarettes in the United Kingdom 38
2.5 Challenges and opportunities associated with comprehensive youth-focused tobacco control policies 39
2.5.1 Challenges to the adoption and effectiveness of TRP regulatory policies designed to protect CYA 39
2.5.1.1 Reluctance to introduce TRP policies 39
2.5.1.2 Compliance and enforcement 39
2.5.1.3 Rapidly evolving TRP market adapted to policies and policy loopholes 40
2.5.1.4 Challenges to prioritizing regulation of products for the greatest impact and to ensure equity 40
2.5.1.5 Concern that regulating products that appeal to CYA could limit switching attempts to newer TRP for adults who smoke 40
2.5.2 Opportunities and methods for overcoming challenges to ensuring comprehensive, effective TRP regulatory policies that protect CYA 41
2.5.2.1 Stakeholder education about the benefits of youth-focused TRP regulatory policies and anticipated secondary impacts on adults 41
2.5.2.2 Designing and implementing policies that are comprehensive, straightforward and adaptable to avoid loopholes and the burden on regulators 41
2.5.2.3 Prioritizing regulatory activities that target populations and products according to the principles of "anticipated impact and equity" 42

2.6 Discussion and conclusions 43
2.7 Research gaps, priorities for regulation and surveillance needs 44
2.7.1 Research gaps 44
2.7.2 Priorities for youth-focused tobacco control and regulation 45
2.7.2.1 Develop and implement a comprehensive approach to reducing all aspects of TRP use by CYA 45
2.7.2.2 Reduce global health disparities associated with smoked tobacco use or smokeless tobacco by CYA without future increase in CYA use of other more recent TRP 45
2.7.2.3 Implement and increase the effectiveness of youth-focused TRP regulatory policies 46
2.7.3 Surveillance needs and recommendations 46
2.7.3.1 Identify factors that contribute to high prevalence of use of TRP by CYA. 46
2.7.3.2 Increase surveillance of emerging TRP classes, including HTPs, nicotine pouches, other nicotine products (e.g. nonmedicinal flavoured commercial nicotine gums and mints), and nicotine analogue products 46
2.8 Policy recommendations 47
2.8.1 To prevent use of and addiction to TRP by CYA, the following regulatory actions aligned with the WHO FCTC are recommended. 47
2.8.2 Considerations in adopting and implementing CYA-focused regulatory policies to improve their impact 48
References 50

3. Flavours in tobacco and nicotine products: new developments, implications and regulation 63

Abstract 64
3.1 Background 64
3.2 Methods 66
3.3 Epidemiology of flavoured products: frequency, patterns and reasons for use by sociodemographic variables 66
3.3.1 Updates on electronic nicotine and non-nicotine delivery systems 66
3.3.2 Updates on conventional smoked and smokeless tobacco products 68
3.3.3 Nicotine pouches 69
3.3.4 Heated tobacco products 70
3.4 Characteristics, properties and health effects of common flavours and implications for public health 70
3.4.1 Global definitions of flavours 70
3.4.2 Emergence of flavours without a traditional "taste" (e.g. synthetic coolants) 71
3.4.2.1 Chemical and physical properties of emerging synthetic flavouring agents 72
3.4.2.2 Toxicity of emerging synthetic flavouring agents 72
3.5 Marketing of flavours in tobacco and nicotine products 73
3.5.1 Conventional marketing of flavoured tobacco products 73
3.5.2 Newer marketing strategies for flavoured tobacco and nicotine products 74
3.6 Effects of flavours on appeal, abuse liability, experimentation, uptake and sustained use 76
3.6.1 Appeal 76
3.6.1.1 How flavour appeal supports experimentation and uptake 76
3.6.1.2 How flavour appeal differs for youth, young adults and adults who use tobacco (and who may be attempting to quit) 77
3.6.2 Abuse liability 77

3.6.2.1 Abuse liability and sustained use 78
3.6.2.2 Consideration of abuse liability in specific populations 78
3.6.2.3 Abuse liability of emerging flavoured products 79
3.6.2.4 How the form of nicotine impacts the appeal and abuse liability of flavours 79
3.7 Regulation of flavoured products 80
3.7.1 Case study: Netherlands (Kingdom of the) 89
3.7.2 Impact of regulation of specific flavoured products 90
3.8 Discussion 93
3.9 Research gaps, priorities and questions 93
3.10 Recommendations 95
References 96

4. Science of sugars in tobacco and nicotine products and regulatory recommendations, an update 111
Abstract 112
4.1 Background 112
4.2 Methods 114
4.3 Sources and levels of sugars in tobacco and nicotine products 114
4.3.1 Types of sugars naturally present in tobacco and the impact of processing 115
4.3.2 Sugars and sweeteners added during processing 116
4.3.3 Methods for measuring sugars and sweeteners in tobacco and nicotine products 116
4.3.4 Types and levels of sugars in various tobacco and nicotine products 117
4.3.4.1 Smoked products 118
4.3.4.2 Smokeless tobacco 119
4.3.4.3 E-cigarettes and heated tobacco products 119
4.3.4.4 Nicotine pouches 120
4.4 Chemistry of the thermal degradation of sugars and sweeteners 120
4.5 Contribution of sugars to the abuse liability of tobacco and nicotine products 121
4.5.1 Contribution of sugars to the attractiveness of tobacco and nicotine products 121
4.5.2 Contribution of sugars to the addictiveness of tobacco and nicotine products 122
4.5.2.1 Effects on the bioavailability of nicotine in product emissions 122
4.5.2.2 Contribution to the addictive properties of nicotine 123
4.6 Implications of sugars and sweeteners for the toxicity of tobacco and nicotine products 124
4.6.1 Contribution of sugars and sweeteners to toxic emissions from various tobacco and nicotine products 124
4.6.1.1 Contribution of sugars to cigarette smoke emissions 124
4.6.1.2 Contribution of sugars and sweeteners to waterpipe tobacco smoke emissions 124
4.6.1.3 Contribution of sugars and sweeteners to e-cigarette emissions 125
4.6.1.4 Contribution of sugars and sweeteners to heated tobacco product emissions 125
4.6.2 Implications of toxicity for people who smoke or use heated tobacco and nicotine products 125
4.6.3 Implications of toxicity for people who use smokeless tobacco and nicotine products 126
4.7 Effects of sugars on perception and use of tobacco and nicotine products 127
4.8 Tobacco industry research on sugars in tobacco products 128
4.8.1 Industry approach to testing the toxicity of ingredients 129
4.8.2 Findings of industry research on toxicity 129
4.8.3 Limitations of industry research on toxicity 130
4.8.4 Exploration or use of alternatives to sugars by the industry 131
4.9 Regulation of sugars 132

4.9.1. Examples of relevant regulation of tobacco and nicotine products 132
4.9.2 Challenges associated with regulating sugars in tobacco and nicotine products 133
4.10 Summary and conclusions 134
4.11 Areas for research and future directions 135
4.12 Policy recommendations 136
References 137

5. Cigarette filters: implications for smoking behaviour, health effects and the environment 148
Abstract 149
5.1 Introduction 150
5.1.1 Scope and aim 151
5.1.2 Methods 151
5.2 History, marketing and types of filters 152
5.2.1 Development and introduction of cigarette filters 152
5.2.2 Marketing and consumption patterns of filtered cigarettes 152
5.2.3 Types of cigarette filters 153
5.3 Effects of filters on smoke emissions, smoking intensity and health 154
5.3.1 Effects of filter ventilation 154
5.3.2 Effects of charcoal filters 154
5.3.3 Health implications of filters 155
5.4 Perceptions of cigarette filters 156
5.4.1 Misconceptions of the effectiveness of filters in reducing human harms 156
5.4.2 Public knowledge about filters and attitudes towards regulatory policies 156
5.5 Environmental impacts of discarded cigarette filters 157
5.5.1 Chemical toxicity of cigarette butt waste 157
5.5.2 Plastic pollution from cigarette filters 157
5.5.3 Biodegradability of filters 158
5.5.4 Recycling schemes 159
5.5.5 Human health implications of discarded cigarette butts 159
5.5.5.1 Bioaccumulation 159
5.5.5.2 Cigarette butt ingestion 159
5.6 Summary 160
5.7 Conclusions 161
5.8 Research gaps, priorities and questions 161
5.9 Regulatory options regarding cigarette filters 162
5.9.1 Policy options 162
5.9.2 The current regulatory environment 162
5.10 Main recommendations 163
References 163

6. Evolving design, additives and accessories for cigarettes and effects on addictiveness, attractiveness and toxicity 171
Abstract 172
6.1 Introduction 172
6.2 Methods 173
6.3 History of important cigarette design variations 174
6.3.1 Elasticity 174
6.3.2 Filters 174
6.3.3 Filter ventilation 175

6.3.4 Menthol 176
6.3.5 Charcoal 176
6.3.6 Slim and superslim cigarettes 177
6.3.7 Roll-your-own 177
6.3.8 Pseudocigarettes 178
6.4 Emerging issues relevant to cigarette design 179
6.4.1 Synthetic coolants to replace menthol 179
6.4.2 Synthetic nicotine 180
6.4.3 Nicotine analogues 181
6.4.4 Substitute fillers 182
6.4.5 Filter (flavour) capsules 185
6.5 Aftermarket modifiers of commercial cigarettes 185
6.5.1 Flavour cards or inserts 186
6.5.2 Filter modifiers 186
6.5.3 External filters 186
6.5.4 Smoking devices 187
6.6 Discussion 188
6.7 Recommendations 189
6.7.1 Short-term 189
6.7.2 Medium- and long-term 190
References 190

7. Aldehydes and metals in e-liquids as potential targets for regulation 204
Abstract 204
7.1 Background 205
7.2 Methods 206
7.3 Overview of e-liquid composition 206
7.3.1 Toxicants in e-liquids 207
7.4 Aldehydes in e-liquids 208
7.4.1 Types and content of aldehydes in e-liquids 208
7.4.2 Characteristics of aldehydes in e-liquids 208
7.4.3 Determination of aldehydes in e-liquids 212
7.4.4 Implications of the presence of aldehydes in e-liquids 213
7.4.4.1 Attractiveness 213
7.4.4.2 Addictiveness 213
7.4.4.3 Possible effects on toxicants in e-cigarette aerosol 213
7.5 Metals in e-liquids 214
7.5.1 Types and content of metals in e-liquids 214
7.5.1.1 Factors associated with higher metal concentrations in e-liquids 216
7.5.1.2 Transfer of metals from e-liquids to aerosols 217
7.5.2 Characteristics of metals in e-liquids 218
7.5.3 Determination of metals in e-liquids 219
7.5.4 Toxicity implications of the presence of metals in e-liquids 220
7.5.4.1 Exposure of e-cigarette users to metals 220
7.5.4.2 Toxic and carcinogenic effects of metals in e-cigarettes 221
7.6 Regulation of aldehydes and metals in nicotine and tobacco products 223
7.7 Summary and conclusions 224
7.8 Research directions 225
7.9 Policy recommendations 225
References 225

8. Smokeless tobacco: a complex landscape, product regulation and considerations for the future 233
Abstract 233
8.1 Introduction 234
8.2 Methods 237
8.3 Overview of products 237
8.3.1 Types of SLT products 237
8.3.2 Characteristics of SLT products 238
8.4 A complex landscape 242
8.4.1 Case studies of product marketing 244
8.4.2 Health impact and cessation 245
8.5 Regulation and future considerations 248
8.5.1 Regulatory challenges 248
8.5.2 Regulatory landscape 249
8.5.3 Examples of studies on regulation of SLT 251
8.5.4 Opportunities and considerations for the future 252
8.6 Research gaps, priorities and questions 254
8.7 Policy recommendations 256
References 258

9. Tobacco and nicotine product characteristics and relevant standards 265
Abstract 266
9.1 Background 266
9.2 Methods 267
9.3 How manufacturers carefully design tobacco and nicotine products to influence their attractiveness, addictiveness and toxicity 268
9.3.1 Attractiveness 268
9.3.1.1 Flavours 268
9.3.1.2 Additives that reduce harshness and contribute to flavour 269
9.3.1.3 Ingredients added to imply health benefits or stimulating effects 270
9.3.1.4 Cigarette filters and filter ventilation 271
9.3.1.5 Product dimensions (not including packaging) 271
9.3.1.6 Attractive design features (not including packaging) 271
9.3.2 Addictiveness 272
9.3.2.1 Total nicotine content as a function of tobacco type 272
9.3.2.2 Total nicotine content as a function of product unit size 272
9.3.2.3 Product characteristics that alter nicotine bioavailability in cigarette smoke 273
9.3.2.4 Unprotonated nicotine in smokeless tobacco products 274
9.3.2.5 Nicotine forms in ENDS and nicotine pouches 274
9.3.3 Toxicity 275
9.3.3.1 Tobacco type 275
9.3.3.2 Additives, including menthol 275
9.3.3.3 Product dimensions 276
9.3.3.4 Cigarette filters 277
9.3.3.5 Filter ventilation 277
9.3.3.6 ENDS device characteristics 277
9.3.4 Careful balancing of product design features by manufacturers 278
9.4 Product standards and how can they be used to reduce use of tobacco and nicotine products 278

9.4.1 Use of product standards to reduce demand for tobacco and nicotine 278
9.4.1.1 Product standards to reduce the attractiveness of tobacco and nicotine products 279
9.4.1.2 Product standards to reduce potential dependence on and addictiveness of tobacco and nicotine products 281
9.4.1.3 Product standards to reduce the toxicity of tobacco and nicotine products 282
9.5 Industry tactics 283
9.5.1 Circumvention of flavour bans 284
9.5.2 Circumvention of regulations on nicotine products and/or nicotine standards 284
9.6 Impact and measurement of the effectiveness of product standards 285
9.7 Implications of findings and research directions 285
9.7 Policy recommendations 287
References 288

10. Overall recommendations 300
10.1 Main recommendations 302
10.2 Significance for public health policies 304
10.3 Implications for WHO programmes 305
References 306

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Abbreviations and acronyms

BaP	benzo[*a*]pyrene
CMR	carcinogenic, mutagenic or teratogenic
COP	Conference of the Parties
COVID-19	coronavirus disease 2019
CRST	Center for Rapid Surveillance of Tobacco
CYA	children and young adults
2,4-DNP	2,4-dinitrophenylhydrazone
ENDS	electronic nicotine delivery systems
ENNDS	electronic non-nicotine delivery systems
EU	European Union
FAO	Food and Agricultural Organization of the United Nations
FDA	Food and Drug Administration (USA)
FEMA	Food and Extracts Manufacturers Association
GC-MS	gas chromatography–mass spectrometry
GCC	Gulf Cooperation Council
HTP	heated tobacco products
IARC	International Agency for Research on Cancer
IITRI	IIT Research Institute
ISO	International Organization for Standardization
ITC	International Tobacco Control
LC	liquid chromatography
LD50	median lethal dose
LMIC	low- and middle-income countries
LOD	limit of detection
MNBA	4-(methylnitrosamino)butyric acid
MNPA	3-(methylnitrosamino)propionic acid
N/A	not applicable
NAB	*N*′-nitrosoanabasine
NAT	*N*′-nitrosoanatabine
NAzCA	*N*-nitrosoazetidine-4-carboxylic acid
NNAL	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol
NNN	*N*′-nitrosonornicotine
NNK	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone
NSAR	*N*-nitrososarcosine
NTP	National Toxicology Program
PAH	polycyclic aromatic hydrocarbons
PATH	Population Assessment of Tobacco and Health

PMTA	premarket tobacco product application
POS	point-of-sale
SLT	smokeless tobacco
TNCO	tar, nicotine and carbon monoxide
TobLabNet	WHO Tobacco Laboratory Network
TobReg	WHO Study Group on Tobacco Product Regulation
TPW	tobacco product waste
TRP	tobacco and related products
TRPM-8	transient receptor potential melastatin subtype 8
TSNA	tobacco-specific nitrosamines
TUS-CPS	Tobacco Use Supplement to the Current Population Survey
USA	United States of America
UV	ultraviolet absorbance
WHO	World Health Organization
WHO FCTC	WHO Framework Convention on Tobacco Control
WNTD	World No Tobacco Day
WS	Wilkinson-Sword

1. Introduction

Tobacco use remains one of the leading preventable causes of premature death, killing over 7 million people a year globally, over 1.6 million of the deaths being due to exposure to tobacco smoke *(1)*. Despite significant progress in reducing tobacco consumption through comprehensive tobacco control policies and public health campaigns, the tobacco and nicotine product landscape remains dynamic and challenging *(2)*. In addition to creating new and emerging products, the tobacco and nicotine industries continuously modify and enhance existing products, making them more attractive and appealing through changes in design, flavour, and delivery mechanisms. They also market them through numerous channels, especially targeting children and young people. Therefore, effective tobacco product regulation is an essential component of a comprehensive tobacco control programme *(3)*.

Product regulation has an important role to play in reducing the demand for tobacco *(3)*. Regulation includes the contents and emissions, identified by mandated testing, disclosure of test results, setting limits as appropriate, disclosure of information on products and imposition of standards for product packaging and labelling. Tobacco product regulation is covered under Articles 9, 10 and 11 of the WHO FCTC *(4)* and in the partial guidelines for implementation of Articles 9 and 10 of the WHO FCTC *(5)*. Other WHO resources to provide support to Member States include the basic handbook on tobacco product regulation *(3)* and the handbook on building laboratory testing capacity *(6)*, and relevant WHO publications, which are freely available on the WHO Tobacco Free Initiative Unit website *(7)*. Additionally, the WHO Study Group on Tobacco Product Regulation (TobReg) has published reports and advisory notes that provide guidance on several aspects of regulating tobacco products and non-therapeutic nicotine products.

The Study Group was formally constituted by the WHO Director-General in 2003 to address gaps in the regulation of tobacco products. Its mandate is to provide evidence-based recommendations on policy for tobacco product regulation to the Director-General. TobReg is composed of national and international scientific experts on product regulation, treatment of tobacco dependence, toxicology and laboratory analyses of tobacco product ingredients and emissions. The experts are from countries in all six WHO regions (8). As a formal entity of WHO, TobReg submits technical reports that provide the scientific basis for tobacco product regulation to the WHO Executive Board, through the Director-General, to draw the attention of Member States to WHO's work in this field. The reports, which are part of the WHO Technical Report Series, include previously unpublished background papers that synthesize published scientific literature and have been discussed, evaluated and reviewed by TobReg.

In accordance with Articles 9 and 10 of the WHO FCTC, relevant decisions of the COP to the WHO FCTC and relevant WHO reports submitted to the COP, TobReg reports identify evidence-based approaches to regulating all forms of tobacco, nicotine and related products, including conventional cigarettes and new and emerging products such as electronic nicotine delivery systems, electronic non-nicotine delivery systems, heated tobacco products and nicotine pouches. These reports, now considered to be WHO technical products (formally known as global public health goods) respond to World Health Assembly resolutions WHA53.8 (2000), WHA53.17 (2000) and WHA54.18 (2001). WHO technical products or global public health goods are initiatives developed or undertaken by WHO that are of benefit either globally or to many countries in several regions *(9)*. This designation presents a unique opportunity for TobReg to engage directly with Member States and contribute to national, regional and global policy.

The twelfth meeting of TobReg, held on 10–13 December 2024 in Barcelona, Spain, was hosted by the WHO Collaborative Centre for Tobacco Control, Tobacco Control Unit, Catalan Institute of Oncology, L'Hospitalet de Llobregat, Spain, and organized by the Tobacco Free Initiative Unit of the WHO Department of Health Determinants, Promotion, and Prevention. Thirty-five participants, including TobReg members, WHO staff, the Secretariat of the WHO FCTC and invited experts, discussed the scientific literature on pertinent topics in product regulation, including emerging issues, according to Member States' requests to WHO, gaps identified in previous TobReg reports, engagement with national focal points for tobacco control and requests to the COP. The report also addresses topics previously considered by the Global Tobacco Regulators Forum and WHO consultations with various stakeholders, including Member States, such as flavours, sugars and cigarette filters, which continue to pose challenges to regulators, as their role is to increase product appeal and they are accompanied by misleading information that leads to misconceptions about perceived risks and harm. The tobacco, nicotine and related industries are therefore exploiting regulatory loopholes for commercial gain at the expense of health, especially that of children, adolescents and young people. In response to these challenges and repeated requests from Member States for technical assistance and authoritative guidance on emerging issues in tobacco and nicotine product regulation, the report includes papers on the contents and characteristics of tobacco and nicotine products that enhance their attractiveness and appeal, with a particular focus on their impact on children and young people. The meeting thus provided a platform for discussing nine background papers:

- Regulation of tobacco and related products. Priorities for the protection of children and young people
- Flavours in tobacco and nicotine products: new developments, implications and regulation

- Science of sugars in tobacco and nicotine products and regulatory recommendations, an update
- Cigarette filters: implications for smoking behaviour, health effects and the environment
- Evolving design, additives and accessories for cigarettes and effects on addictiveness, attractiveness and toxicity
- Aldehydes and metals in e-liquids as potential targets for regulation
- Waterpipe tobacco: characteristics, toxicity and regulation
- Smokeless tobacco: a complex landscape, product regulation and considerations for the future
- Tobacco and nicotine product characteristics and relevant standards

The seventh background paper was included to report on new developments, science and regulation of waterpipe tobacco since the Study Group's most recent report on the topic, in its seventh report. The paper was, however, not included in the current report, as there was insufficient new information for its inclusion. The report therefore contains eight background papers.

The first paper, on young people, sets the stage for many of the subsequent papers. It covers factors that drive use of tobacco and nicotine products by the young, with emphasis on those variables that increase attractiveness and appeal. Reducing the appeal and attractiveness of harmful tobacco and nicotine products helps to safeguard the health and well-being of children and young people. These concepts are examined in more detail in papers 2–5, which cover flavours, sugars and sweeteners, and filters and other design features. The fourth paper, on cigarette filters, not only recognizes cigarette filters as a marketing tool which propagates misinformation and appeal, but also addresses cigarette filters from an environmental perspective, in relation to Article 18 of the WHO FCTC. The paper on aldehydes and heavy metals in e-liquids presents the current state of knowledge on their presence in e-cigarette liquids and the implications for product attractiveness, addictiveness and toxicity. The paper on smokeless tobacco outlines the substantial challenges that these products pose for regulation and stresses the importance of applying, enforcing and monitoring control policies, programmes and interventions similar to those applied to cigarettes and other smoked tobacco products, with the same rigour. The paper on product standards provides relevant information on the basis for setting product standards and explores tobacco control regulatory processes and systems that could enhance the effectiveness of product standards.

The content of the eight background papers is based on requests by Members States in all six WHO regions, the knowledge of the WHO Secretariat, subject matter experts, resource persons and the Study Group and relevant

literature. The information in the background papers updates current knowledge to advance tobacco and nicotine product regulation and inform national and global policy. The papers were prepared by experts according to their terms of reference or to an outline drawn up by the WHO Secretariat for each paper and were reviewed and revised by TobReg members and by expert reviewers identified by WHO. The period of the literature search is indicated in each paper; for most, this was the second half of 2024. The papers were reviewed several times before and after the meeting by independent technical experts, the WHO Secretariat, people in other relevant WHO departments, colleagues at regional offices and members of the Study Group. Reviewers' comments were carefully evaluated and taken into consideration prior to compilation and finalization of the report by the Study Group. All experts and other participants in the meeting, including members of the Study Group, were required to complete declarations of interests, which were evaluated by WHO.

The WHO Secretariat, in consultation with the Study Group, invited experts who contributed to discussions and provided the most recent empirical scientific evidence and regulations on the topics under consideration. This tenth report of TobReg on the scientific basis of tobacco product regulation is designed to guide Member States in achieving the most effective, evidence-based means for bridging regulatory gaps in tobacco control and in developing coordinated regulatory frameworks for tobacco, nicotine and related products. Additionally, the report identifies future areas of work on regulation in countries, indicating a strategy for continued technical support to Member States. It does not cover all the emerging issues related to tobacco and nicotine product regulations, such as synthetic additives, analogues and synthetic flavour replacements. As agreed by consensus in the Study Group, several recommendations in the report were tabled at the 157th WHO Executive Board Meeting in May 2025, where they received support from Member States *(10)*.

The report comprises this introduction, the eight papers on topics pertinent to tobacco control regulations and a summary of the recommendations in each paper. The recommendations, which represent syntheses of complex research and evidence, are intended to promote international coordination, capacity-building and adoption of best practices in product regulation in all WHO regions. The recommendations, based on sound science, represent a ready resource for Member States in implementing the WHO FCTC. In view of the aggressive promotion of tobacco and nicotine products globally, the Study Group urges Member States to continue to focus on evidence-based measures to reduce tobacco use, as outlined in the WHO FCTC, and to avoid distraction by the tobacco, nicotine and related industries.

Future reports of the Study Group will address other aspects of product regulation, including emerging issues that directly impact tobacco control, as guided by the regulatory needs of countries and pertinent issues in product regulation. The reports will also address the broad range of non-therapeutic

tobacco and nicotine products on global markets and factors with regulatory implications for product regulation, especially those that affect the attractiveness, addictiveness and toxicity of these products. This will ensure continued, timely technical support to all countries by the WHO Secretariat.

In summary, the outcomes of TobReg's deliberations and its recommendations will improve Member States' understanding of the evidence on the topics considered in this report, contribute to the body of knowledge on product regulation, inform WHO's work, especially in providing technical support to Member States, and keep Member States, regulators, civil society organizations, research institutions and other interested parties up to date on product regulation through various platforms. Thus, the Study Group's activities will contribute to meeting Sustainable Development Goal 3.a: to strengthen implementation of the WHO FCTC *(9)*.

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2. Regulation of tobacco and related products. Priorities for the protection of children and young people

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Contents

Abstract
2.1 Background
2.1.1 Introduction
2.1.2 WHO resources on prioritizing protection of children and young people
2.1.2.1 World No Tobacco Day (WNTD)
2.1.2.2 Nicotine- and tobacco-free schools: Policy development and implementations toolkit
2.1.2.3 Decisions of the COP to the WHO FCTC
2.1.2.4 WHO call to action
2.1.2.5 United Nations Convention on the Rights of the Child
2.1.3 Scope and aim of the paper
2.2 Methods
2.3 Prevalence and determinants of TRP use by CYA
2.3.1 Prevalence of TRP use by CYA
2.3.1.1 Overall use of one or more TRP
2.3.1.2 Cigarettes
2.3.1.3 Hookah or waterpipe tobacco
2.3.1.4 Cigars and cigarillos
2.3.1.5 HTP
2.3.1.6 E-cigarettes
2.3.1.7 Smokeless tobacco products
2.3.1.8 Nicotine pouches
2.3.1.9 Other nicotine products
2.3.1.10 Combined use of two or more TRP
2.3.1.11 Differences in TRP use by demographic and other dimensions of diversity
2.3.2 Factors that drive TRP use and appeal among CYA
2. 3.2.1 Flavours
2.3.2.2 Non-flavour additives or other modifications that increase sensory appeal
2.3.2.3 Design for discreet use and concealability
2.3.2.4 Convenience and low cost
2.3.2.5 Product design that attracts CYA by resembling CYA-oriented products (including food and toys)
2.3.2.6 Unique CYA appeal of nicotine products, synthesized nicotine and nicotine analogue products
2.3.3 Abuse liability of tobacco and related products
2.3.3.1 Nicotine concentration
2.3.3.2 Method of administration
2.3.3.3 Additives and manufacturing processes that change pH or enhance nicotine absorption
2.3.3.4 Flavours and other sensory enhancers
2.3.3.5 Nicotine analogues and other non-nicotine psychoactive compounds

2.3.3.6 Device power
2.3.4 Impact of TRP marketing on use by CYA
2.4 Prioritization of protection of children and young people
2.4.1 Tools
2.4.2 Surveillance
2.4.2.1 Surveys
2.4.2.2 Observations and sales in "brick-and-mortar" retailers
2.4.2.3 Surveillance of retailers on the Internet
2.4.2.4 CYA advocates and advisory groups
2.4.2.5 Surveillance of social media
2.4.3 Regulation of TRP to protect CYA
2.4.3.1 Overview and regulatory mechanisms
2.4.3.2 Comprehensive ban on manufacture and sale to CYA of all TRP or all TRP in a specific product class
2.4.3.3 Minimum age purchase laws
2.4.3.4 Restrictions on sales to CYA of TRP with specific product characteristics or design features that attract CYA
2.4.3.5 Marketing, packaging and advertising of TRP
2.4.3.6 Sales and pricing policies to limit access and affordability for CYA
2.4.3.7 Warning label requirements
2.4.3.8 Banning use of TRP in public settings
2.4.4 Country case studies
2.4.4.1 Cigarettes in Australia
2.4.4.2 E-cigarettes in the USA
2.4.4.3 E-cigarettes in the United Kingdom
2.5 Challenges and opportunities associated with comprehensive youth-focused tobacco control policies
2.5.1 Challenges to the adoption and effectiveness of TRP regulatory policies designed to protect CYA
2.5.1.1 Reluctance to introduce TRP policies
2.5.1.2 Compliance and enforcement
2.5.1.3 Rapidly evolving TRP market adapted to policies and policy loopholes
2.5.1.4 Challenges to prioritizing regulation of products for the greatest impact and to ensure equity
2.5.1.5 Concern that regulating products that appeal to CYA could limit switching attempts to newer TRP for adults who smoke
2.5.2 Opportunities and methods for overcoming challenges to ensuring comprehensive, effective TRP regulatory policies that protect CYA
2.5.2.1 Stakeholder education about the benefits of youth-focused TRP regulatory policies and anticipated secondary impacts on adults
2.5.2.2 Designing and implementing policies that are comprehensive, straightforward and adaptable to avoid loopholes and the burden on regulators
2.5.2.3 Prioritizing regulatory activities that target populations and products according to the principles of "anticipated impact and equity"
2.6 Discussion and conclusions
2.7 Research gaps, priorities for regulation and surveillance needs
2.7.1 Research gaps
2.7.2 Priorities for youth-focused tobacco control and regulation
2.7.2.1 Develop and implement a comprehensive approach to reducing all aspects of TRP use by CYA

2.7.2.2 Reduce global health disparities associated with smoked tobacco use or smokeless tobacco by CYA without future increase in CYA use of other more recent TRP
2.7.2.3 Implement and increase the effectiveness of youth-focused TRP regulatory policies
2.7.3 Surveillance needs and recommendations
2.7.3.1 Identify factors that contribute to high prevalence of use of TRP by CYA.
2.7.3.2 Increase surveillance of emerging TRP classes, including HTPs, nicotine pouches, other nicotine products (e.g. nonmedicinal flavoured commercial nicotine gums and mints) and nicotine analogue products
2.8 Policy recommendations
2.8.1 To prevent use of and addiction to TRP by CYA, the following regulatory actions aligned with the WHO FCTC are recommended
2.8.2 Considerations in adopting and implementing CYA-focused regulatory policies to improve their impact
References

Abstract

This paper addresses priorities for youth-focused regulation of tobacco and related products (TRP) by synthesizing the literature on use trends, products, marketing approaches, surveillance strategies and regulator activities to reduce TRP use by children and young adults (CYA). We found that the prevalence of use of TRP by CYA differs among countries and types of TRP, smoked tobacco continuing to be problem in many regions and e-cigarette and nicotine pouch use becoming common in several countries. Marketing in venues popular among CYA (e.g. social media, online video games), sweet, cooling and fruity flavours, product designs that allow discreet use or resemble toys, perceptions of low harm for some TRP and TRP sales operations that increase accessibility each increase TRP use and addiction in CYA. The literature indicates recommendation of the following youth-focused TRP (including smoked tobacco) regulation and control activities: (1) bans on the sale of all TRP with flavours, sensory-modifying additives, designs that enable discreet use or resemble toys and other product characteristics that increase appeal and abuse liability to CYA; (2) bans on promotion and advertising of all TRP, including all digital and non-digital media, to reduce TRP use by CYA; (3) mandating labels on TRP packaging and products with health warnings, and relevant ingredients and emissions and ensure labels and packaging does not contain quantitative or qualitative statements that might imply that one brand is less harmful than another; (4) minimum age purchase laws, no Internet sales, taxation and limiting sales to establishments that require customers to be aged ≥ 21 years to enter; (5) overcoming challenges to enforcement and designing policies without loopholes; and (6) multi-modal industry monitoring and surveillance of use of TRP by CYA to guide swift, equitable regulatory actions.

Keywords: youth, protection, initiation, tobacco, nicotine, marketing

2.1 Background

2.1.1 Introduction

Death and disability from the use of TRP that contain tobacco, nicotine and/or other psychoactive nicotine analogue compounds sold on the commercial market can be reduced by regulation. Prioritizing regulatory activities that reduce use of TRP by CYA is vital for tobacco control. Nearly all individuals who regularly use TRP start in adolescence or during young adulthood (1). The evolving market and development of increasingly diverse TRP and marketing strategies that attract CYA have increased the prevalence of CYA TRP use to that of adults or exceeded it in many countries, especially of TRP introduced in the 21st century ("emerging" TRP) (2). This paper addresses current priorities for TRP regulation to protect CYA.

2.1.2 WHO resources on prioritizing protection of children and young people

To contextualize this paper, we first summarize recent activities by WHO and other organizations for preventing TRP use and other negative impacts in CYA.

2.1.2.1 World No Tobacco Day (WNTD)

The protection of young people has been woven into the theme and aims of the WNTD campaigns, launched on 31 May of each year. The theme of the WNTD 2025 campaign is "Unmasking the appeal: exposing industry tactics on tobacco and nicotine products", which addresses one of the primary public health challenges today – the attractiveness of tobacco, nicotine and related products, particularly to CYA *(3)*. A previous WNTD theme directly relevant to addressing CYA was "Protecting children from tobacco industry interference", with the launch of a joint report by WHO and Stopping Tobacco Organizations and Products (STOP), a global tobacco industry watchdog, "Hooking the next generation", which describes how TRP manufacturers and marketers design products and marketing campaigns to attract CYA to TRP use *(4)*. Previous WNTD campaigns also addressed the protection of children working in unsafe environments in growing tobacco and the issue of CYA who are exposed to the adverse environmental consequences of TRP manufacture and use. They have identified the importance of prevention, given the challenge of quitting TRP after lifelong use and addiction, and called on all young people to build a movement for a tobacco-free generation and for schools to adopt tobacco- and e-cigarette-free campuses.

2.1.2.2 Nicotine- and tobacco-free schools: Policy development and implementation toolkit

A WHO toolkit supports implementation of nicotine- and tobacco-free school policies. It consists of four parts: 1, banning TRP use on school grounds; 2, banning sales of TRP near schools; 3, prohibiting direct and indirect advertising and promotion of TRP near schools; and 4, banning any form of sponsorship by or interaction with the TRP industries *(5)*.

2.1.2.3 Decisions of the COP to the WHO FCTC

At the tenth session of the COP in Panama in 2024, Parties adopted the Panama Declaration (FCTC/COP10(11)) *(6)*, which commits them to

> strengthen their efforts to increase public awareness by providing accurate information on the nicotine addiction and health risks and consequences associated with the use of novel and emerging nicotine and tobacco products, in particular among the children and youth.

Further, in their decision on implementation of Article 18 of the WHO FCTC (FCTC/COP10(14)) *(7)*, Parties noted that women and children are often exposed to health risks while handling green tobacco leaves and to tobacco smoke during curing. In addition, WHO FCTC COP decision FCTC/COP10(23) recommends that Parties ensure comprehensive bans on tobacco advertising, promotion and sponsorship and their enforcement as an integral part of protection of young people online and to promote a safer Internet *(8)*. COP sessions back to 2012 also prioritized protection of CYA from a variety of negative consequences related to using and working in the manufacture of TRP, including preventing use of emerging TRP and taxation policies to reduce use.

2.1.2.4 WHO call to action

In December 2023, WHO issued a call to action on e-cigarettes *(9)*, noting that urgent, strong, decisive action should be taken to prevent uptake of e-cigarettes and to counter addiction to nicotine vaping to protect children and non-smokers as well as to minimize harm to the health of the overall population. The call to action outlined regulatory approaches for countries to ban the sale of e-cigarettes and for countries that permit commercialization of e-cigarettes as consumer products. The latter include regulation of e-cigarettes to reduce their appeal and their harm to the population and measures to prohibit and prevent sale of e-cigarettes to children. WHO's call to action was accompanied by a technical note that described in detail the availability of e-cigarettes in thousands of flavours, which are particularly attractive to children and young people, how children and young people are aggressively targeted in marketing of e-cigarettes, the alarming increase in uptake of e-cigarettes by young people, and how disposable e-cigarettes (particularly commonly used by youth) have more e-liquid volume per unit, contain more nicotine than e-cigarettes marketed several years previously and are increasingly inexpensive and accessible in some regions *(2)*.

2.1.2.5 United Nations Convention on the Rights of the Child

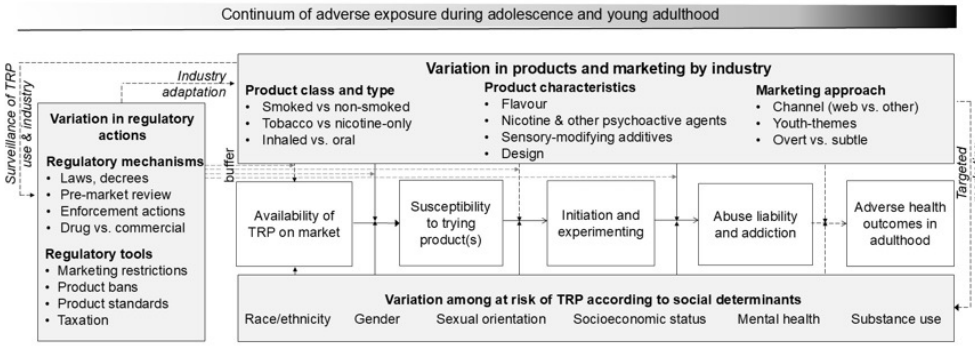
The United Nations Convention on the Rights of the Child *(10)* is a legally binding treaty ratified by 196 countries (as of 31 August 2025). It specifies civil, political, economic, social and cultural rights specific to children, defined as individuals

under the age of 18. WHO policies and education on tobacco regulation are aligned with various articles in the Convention on protecting the interests and health of children.

2.1.3 Scope and aim of the paper

This paper consists of reviews of evidence, current opportunities and challenges and future directions for TRP regulation designed to protect individuals aged ≤ 24 years, aligned with an overarching framework for youth-focused regulation (Fig. 2.1). The framework recognizes the cyclical ecosystem in which industry and policy innovations arise, impact one another and spread locally, nationally and globally.

Fig. 2.1. Framework for youth-focused TRP regulation



The framework recognizes that the TRP industry develops new products and marketing strategies that target CYA and encourages them to try them. The products are often designed to be particularly appealing and addictive to CYA, increasing the risk of initiation and continued use in this population, raising long-term risks for TRP-related addiction, morbidity and premature mortality. The tobacco control community can mitigate the adverse impact of the evolving TRP market by: (i) close surveillance of the market and CYA use of TRP to identify product and marketing features that promote CYA use and that can be targeted by regulation, and (ii) introduction and enforcement of CYA-focused regulation and other measures and activities to protect CYA from appealing TRP and attractive marketing and thus reduce use. The TRP industry has adapted by creating new products and evolved their marketing approaches to elude regulation and to exploit policy loopholes while maintaining the appeal and addictiveness of TRP and perpetuating CYA use. The TRP industry has also reacted to youth-focused regulations by approaches such as moving locations, countries and populations to target vulnerable groups, often defined by race or ethnicity, sexual/gender identity, mental health or socioeconomic status. Consequently, it is critical that the tobacco

control community identify, address and close the loopholes and comprehensively apply TRP regulations and other measures to improve health and avoid TRP-related health disparities.

After a summary of the methods used, the paper presents the results of a targeted review of evidence of the prevalence and modifiable determinants of TRP use and addiction among CYA. Surveillance tools and regulatory activities designed to mitigate TRP use and its impact for CYA are then reviewed. Subsequently, current challenges and opportunities in regulation of TRP to protect CYA are described. After a discussion of the preceding sections, the paper concludes with recommended priorities for research and regulatory activities to reduce the use of and addiction to TRP among CYA, and policy recommendations.

2.2 Methods

A targeted, non-exhaustive search was conducted to address WHO's terms of reference for the paper between June and December 2024. The search included scientific literature in PubMed, Google Scholar and other databases. Relevant conference abstracts and policy documents were included when applicable. Selected industry documents and marketing materials were included for context. The collection of sources was reviewed by the authors to refine the scope of the paper and followed up with additional targeted sources. The final collection of sources was synthesized and organized into thematically homogeneous sections. During the review, data on countries' regulatory measures were updated from the WHO Global Tobacco Epidemic Report 2025 *(11)*, and data on the prevalence of use of TRP were updated in line with WHO global report on trends in prevalence of tobacco use 2000–2024 and projections to 2025–2030 *(12)*.

2.3 Prevalence and determinants of TRP use by CYA

2.3.1 Prevalence of TRP use by CYA

The definitions of specific TRP are listed in Table 2.1. Given the lack of data on the prevalence of CYA TRP use in many countries, especially of certain emerging products, the evidence reviewed below does not provide definitive, exhaustive estimates of prevalence suitable for systematic country-by-country comparisons. Rather, the estimates are intended to provide a general picture of the epidemiology of and international variation in global CYA TRP use, which are strongly influenced by where products are marketed and the corresponding regulations. When available, separate estimates of the prevalence of use are provided for each "class" of TRP. (e.g. cigarettes, cigars and hookah/waterpipe are different product classes.).

Table 2.1. Tobacco-related product classes: description and features that attract youth

	Features that attract youth[a]					
	Flavours	Design for discreet use	Convenient	Design of youth-oriented objects, candy or toys	Non-flavour additives that promote uptake	No tobacco leaves
Inhaled tobacco and nicotine products						
Cigarettes. Shredded tobacco typically containing various chemical additives encased in paper wrapping that are intended for smoking and emit tobacco smoke. Cigarettes are usually manufactured and pre-rolled, often with a filter, or sold as roll-your-own with tobacco filler and paper wrappers sold separately.	•		•		•	
Cigars. Rolls of tobacco encased in tobacco leaf or in a wrapper that contains tobacco intended for smoking and emit tobacco smoke. Cigars differ in size, including large cigars up to 2 cm in diameter to smaller cigars, such as little filtered cigars that resemble pre-rolled cigarettes or cigarillos.	•		•		•	
Bidis. Small hand-rolled cigarette-like products filled with tobacco wrapped in a tendu leaf that are intended for smoking and emit smoke.	•		•		•	
Hookah or waterpipe tobacco. A product that includes tobacco that is usually processed and flavoured, which is smoked through a device that passes smoke emissions through a water chamber and via a hose, from which the emissions are inhaled.	•			•	•	
Pipe tobacco. Loose-leaf tobacco that can contain flavourings and additives designed to be placed in the bowl of a pipe device through which smoke is emitted and inhaled.	•			•	•	
E-cigarette. A product in which a device is used to heat a liquid to create an aerosol that is inhaled by the user, which typically contains nicotine and toxic substances that are harmful to both users and non-users who are exposed to the aerosols second hand; the liquid is often flavoured. E-cigarettes are sold in various sizes, shapes and designs, including devices resembling toys, candy and other objects, and can be rechargeable and/or disposable.	•	•[b]	•[b]	•	•	•
HTP. Tobacco product that produces aerosols containing nicotine and toxic chemicals when the tobacco is heated or when the device containing tobacco is activated. The aerosols are inhaled by users during sucking or smoking a device. They contain the highly addictive substance nicotine, as well as non-tobacco additives, and are often flavoured.	•				•	
Other tobacco and nicotine products						
Smokeless tobacco. Such products are made entirely or partly from tobacco or its extracts and are consumed in unburnt form. They are used in a variety of ways, including being chewed, sucked or just held between the lip and the cheek or gums, applied to the teeth or gums (e.g. topical toothpaste or powder), dissolved in the mouth or applied directly to the skin or other body part.	•		•		•	
Tobacco snus. Pre-portioned, finely shredded tobacco encased in sachets. Snus does not require spitting.	•	•[b]	•	•	•	
Tobacco dissolvables. Products with ground processed tobacco infused into lozenges, strips or sticks that dissolve in the mouth and require no spitting.	•	•[b]	•	•	•	

	Features that attract youth[a]					
	Flavours	Design for discreet use	Convenient	Design of youth-oriented objects, candy or toys	Non-flavour additives that promote uptake	No tobacco leaves
Oral nicotine products without tobacco leaves. Products consumed orally, which contain nicotine, flavourings and other additives but do not contain tobacco leaves. They require no spitting and are not considered to be medications for tobacco use cessation. They include nicotine pouches (pre-portioned sachets with microcrystalline cellulose resembling snus), gums, gummies, lozenges, mints, hard candies and toothpicks.	•	•[b]	•	•	•	•
Topical or intranasal tobacco and nicotine products						
TRP containing tobacco or nicotine that are not administered orally or inhaled include gels (viscous substances containing nicotine administered topically) and dry snuff (finely shredded tobacco administered intranasally).		•	•			•
Nicotine analogue products						
Products including e-cigarettes and nicotine pouches that contain chemical compounds structurally or pharmacologically similar to nicotine (known as nicotine analogues), such as 6-methyl nicotine, which are likely to be psychoactive and addictive.	•	•	•	•	•	•

[a] Some products in the TRP class have youth-appealing features (see text below for a description of the features.)
[b] Certain products in this class might be particularly convenient, low cost and easy to conceal and therefore especially attract youth. They include disposable e-cigarettes that do not require recharging or refilling and nicotine mints and lozenges that can be swallowed.

2.3.1.1 Overall use of one or more TRP

Globally, more than 40 million (10.0%) adolescents aged 13–15 years (12.4% of boys and 7.5% of girls) were estimated to use one or more tobacco-containing products (i.e. any product containing tobacco; excluding e-cigarettes and nicotine pouches) according to surveys conducted in various countries between 2014 and 2024 for the United Nations estimated global population for 2023 *(12)*. The estimated average prevalence of use of one or more tobacco-containing product was highest in the WHO European Region, at 11.6%, followed by the WHO Eastern Mediterranean Region (11.0%) and the WHO Western Pacific Region (10.5%); however, considerable international variation was observed within each region *(12)*.

2.3.1.2 Cigarettes

Globally, an average of 5.1% of adolescents aged 13–15 years reported that they were current cigarette smokers (6.8% of boys and 3.3% of girls) in surveys conducted in various countries between 2014 and 2024, for the United Nations estimated global population for 2023. The average prevalence of current cigarette smoking was highest in the WHO European Region (8.4%), the Western Pacific Region (6.4%) and the Region of the Americas (5.7%) *(12)*. The prevalence in 14–18-year-old

youth in the USA in 2024 of use of cigarettes ever and in the past 30 days was 7.4% and 1.7%, respectively *(13)*. In all the other WHO regions, the estimated average prevalence of current use of cigarettes was about 3–5% *(12)*. The 2019 European School Survey Project on Alcohol and Other Drugs *(14)* found that, on average, 20% of mid-adolescents, aged 16 years, were current cigarette smokers. The prevalence differed by country, from 5.1% in Iceland to 32% in both Bulgaria and Italy.

2.3.1.3 Hookah or waterpipe tobacco

The prevalence of hookah or waterpipe tobacco smoking among youth differs globally. For example, in Bosnia and Herzegovina, 16.1% of schoolchildren aged 13–15 years currently used waterpipes in 2019 *(15)*. In Senegal, the prevalence of current use of waterpipe tobacco by youth aged 13–15 years was 2.2% in 2020 *(16)*. In the USA, 0.7% of middle- and high-school students currently used waterpipe tobacco in 2024 *(17)*. The Global Youth Tobacco Survey in 2015 found that, in many countries in the Eastern Mediterranean Region (e.g. Jordan, Lebanon and Syria), current waterpipe tobacco smoking was more prevalent than cigarette smoking among boys and girls aged 13–15 years *(18,19)*.

2.3.1.4. Cigars and cigarillos

Few studies have been conducted of the use of smoked tobacco products by youth other than cigarettes. In the 2024 National Youth Tobacco Survey in the USA *(17)*, cigars ranked as the fourth most common tobacco product currently used by middle- (0.8%) and high-school (1.5%) students and were more widely used by Black African–American and male youth than by the overall population, among whom cigarillos and little filtered cigars were the most common subtypes of cigars used by young people. A study of Dutch youth aged 13–17 years found that 13.4% and 2.0% reported ever use and current use, respectively, of cigarillos in 2020 *(20)*.

2.3.1.5 HTP

In a meta-analysis of the global prevalence of HTP use covering 42 countries and areas in four WHO regions between 2015 and 2022 *(21)*, the estimated prevalence of HTP use by the general population aged ≥ 9 years was 4.9% (lifetime), 1.5% (current) and 0.8% (daily) during that period. The prevalence of current HTP use by the general population increased from 0.12% in 2015 to 10.6% in 2020 in the WHO Western Pacific Region and from 0% in 2016 to 1.2% in 2020 in the WHO European Region *(22)*.

2.3.1.6 E-cigarettes

Globally, e-cigarette use among adolescents aged 13–15 years was estimated to be 7.2%, with 8.6% among boys and 5.7% among girls. These prevalence estimates correspond to approximately 14.7 million adolescents aged 13–15 years currently

using e-cigarettes – 9.1 million boys and 5.6 million girls. The estimates were derived from surveys conducted in countries in the period 2014–2024 and applied to the United Nations estimated population of each country in 2023 *(12)*. A comparison of adult and adolescent surveys in 64 countries shows a striking skew toward adolescent use of e-cigarettes. On average, the prevalence among 13–15-year-olds was nine times higher than that among adults. In half the countries, the adolescent-to-adult ratio was ≥ 9:1; only six countries reported higher use among adults than adolescents *(12)*. The Global Tobacco Surveillance System indicated that current use of e-cigarettes among young people aged 13–15 years was 8.2–18.4% while that among adults was 0.2–3.4% in Philippines, Romania, Ukraine and Uruguay in 2015–2019 *(23)*. In many countries, such as Albania, Belarus, Dominican Republic, Guam, Morocco, Niue, Oman, Russian Federation and Ukraine, current use of e-cigarettes by 13–15-year-olds was two to three times more prevalent than smoking of conventional cigarettes and that in Paraguay was four times more prevalent *(23)*. E-cigarette use among CYA is increasing in some countries. The number of 16–19-year-olds who currently used e-cigarettes in Canada doubled between 2017 and 2022, and, in England (United Kingdom), the prevalence of current e-cigarette use among secondary school pupils years 7 to 11 (mostly aged 11 to 15) has steadily increased from 2014 to 2021, then stabilized between 2021 and 2023 at around 9%, this is triple the prevalence of current smoking in the same group in 2023 (3%)*(24,25)*. According to the 2019 European School Survey Project on Alcohol and Other Drugs *(14)*, three countries in the WHO European Region, Lithuania, Monaco and Poland, recorded a prevalence of current e-cigarette use of ≥ 30% among 15–16-year-olds.

2.3.1.7 Smokeless tobacco products

In data from 129 countries, representing 66% of WHO Member States and 73% of the global population aged 13–15 years, in various nationally representative school surveys conducted between 2014 and 2024, about 3.4% of this population reported current use of smokeless tobacco products *(12)*. The prevalence was higher among boys (4.0%) than girls (2.8%). The highest prevalence of smokeless tobacco use by these adolescents was observed in the WHO African and South-East Asia regions, both estimated at 4.2%. In the WHO African Region, however, only 47% of the population aged 13–15 years was surveyed, and the results are indicative only. Additional surveys may substantially change the estimated regional average prevalence.

2.3.1.8 Nicotine pouches

Data on use of nicotine pouches are lacking for many countries. In an online multinational cross-sectional survey in 2019 of young people aged 16–19 years, the prevalence of use of nicotine pouches in the past 30 days was 1% in Canada, 1.3% in England (United Kingdom) and 1.5% in the USA *(26)*. In a nationally

representative Dutch survey in 2020, awareness about nicotine pouches among adolescents (13–17 years) was relatively high (9.1%), but only 0.3% had ever used one, and none reported current use *(20)*. In a survey in Great Britain (United Kingdom), the Action on Smoking and Health Smokefree Great Britain Youth Survey 2024 of youth aged 11–18 years, 3.3% reported ever use, of whom 1.2% reported current use *(27)*. In the National Youth Tobacco Survey in the USA, the prevalence of ever use of nicotine pouches by middle- and high-school students (11–18 years) was 1.9% in 2021, which rose significantly to 3.5% in 2024. The prevalence of nicotine pouch use in the past 30 days by middle- and high-school students increased significantly, from 0.8% to 1.9% between 2021 and 2024 *(17)*.

2.3.1.9 Other nicotine products

Commercially marketed nicotine gums, lozenges, gummies, mints, candies and toothpicks have recently been introduced on some markets, especially through online marketing, including in the USA *(28–30)*. An estimated 3.1% of middle- and high-school students (age 11–18 years) in the USA reported ever using one or more of such nicotine products in 2024; 1.2% used the products currently *(13)*. Estimates are not available for other countries.

2.3.1.10 Combined use of two or more TRP

While the data remain scant for many regions of the world, studies indicate that combined use of two or more TRP (cigarettes and other forms of tobacco, nicotine and related products) is common among youth *(17, 31-35)*. Combined use of cigarettes and e-cigarettes was the most common current dual use in several countries. In a study of adolescents aged 13–15 years in 67 countries that provided data for Global Youth Tobacco Surveys in 2014–2019, the prevalence of dual use of cigarettes and e-cigarettes ranged from 0.1% in Cambodia to 13.6% in Poland. In 15 of the 67 countries, the prevalence of dual use of cigarettes and e-cigarettes among adolescents was > 5%. A pooled estimate of prevalence in the 67 countries showed that current dual use of cigarettes and e-cigarettes was five times higher among boys than girls *(31)*. Further, in a study of 15–16-year-olds in 32 countries in Europe in 2019, overall current dual use of cigarettes and e-cigarettes was 6.4% *(32)*. Among 15–16-year-old students in five Nordic countries and one territory (Denmark, Faroe Islands, Finland, Iceland, Norway and Sweden), the most common pattern of current dual use was cigarettes and e-cigarettes, the prevalence being 15–21% in four countries but not in the Faroe Islands or Sweden. In the Faroe Islands, the most common form of dual use was cigarettes and snus (12%). In Sweden, dual use of cigarettes with either snus or e-cigarettes was equally common, both at 11% *(33)*.

"Poly-use", defined as use of several tobacco products, among youth, remains a concern. In the National Youth Tobacco Survey 2024 in the USA of middle- and high-school students, 3.0% reported current use of two or more

tobacco products *(17)*. Of adolescents aged 12–18 years in the Republic of Korea in 2020, 0.7% reported current poly-use (cigarettes, e-cigarettes and HTP) *(34)*. In the USA, an estimated 4.0% of respondents to the 2017 National Youth Tobacco Survey used three or more different tobacco products *(35)*.

2.3.1.11 Differences in TRP use by demographic and other dimensions of diversity

Differences in the prevalence of use of TRP by CYA among and within countries are associated with various demographic factors, including sex/gender, race or ethnicity, sexual orientation, mental health, socioeconomic status and use of other substances *(36,37)*. The prevalence of conventional cigarette smoking among CYA aged 13-15 years was highest in upper–middle-income countries (6.8%), with boys showing the highest rate of all income groups (9.2%). Among girls, the prevalence was highest in high-income countries (6.3%), exceeding both the 2–4% range in other income groups and the average for boys in the same category (5.3%). Smokeless tobacco use among CYA was most common in low-income countries (4.7%), although this estimate is less reliable because of limited survey coverage – only 46% of the group's population in nine countries has been surveyed in the period between 2014-2024. E-cigarette use among CYA was highest in low-income (10.9%) and high-income countries (10.0%). In high-income countries, girls reported more use than boys (10.8% vs 9.2%), while the reverse was observed in low-income countries (5.8% vs 15.8%) *(12)*. Additionally, in most countries, TRP use tends to be more common in males than in females, people who identify as transgender or other non-cisgender identities than in cisgender identities, those with mental health symptoms or conditions and those who use alcohol or other drugs *(38–41)*.

2.3.2 Factors that drive TRP use and appeal among CYA

The common characteristics of TRP marketed by industries that attract CYA are listed in Table 2.1 by TRP class (e.g. cigarettes, cigars, pipes) and CYA-attracting characteristic. In several TRP classes, certain subtypes of products are more likely to be appealing; for example, in the product class of cigarettes, pre-rolled cigarette subtypes are more convenient than roll-your-own subtypes. Such TRP characteristics increase young peoples' susceptibility to trying and initiating use and for continuing use after experimentation (Fig. 2.1). Cross-cutting characteristics that drive CYA appeal are described below.

2.3.2.1 Flavours

Virtually all classes of TRP include products with flavours or flavour enhancements, such as chemical flavouring additives designed to stimulate chemosensory perceptions that mimic sensations produced by flavours in foods. Flavouring chemicals are also added to TRP to elicit a cooling sensation, perceived sweetness

or another element to enhance the experience of using TRP. In addition to flavourings added directly to the consumed product (e.g. on tobacco or in e-liquid), flavours such as sweeteners are placed on the filters of cigars or cigarettes or on the microfibre casing of nicotine pouches or snus products. TRP may be flavoured not with chemical additives but by other manufacturing processes that alter the sensation produced, such as curing or ageing *(42)*. Various flavour categories have been identified in TRP, including fruit, candy, dessert, mint, menthol, alcoholic beverages and flavour combinations.

Studies have shown consistently that flavours increase TRP appeal and use among CYA globally. The universal appeal-enhancing effects of flavours for CYA are due to various mechanisms. Among CYA who have never used TRP, the idea of using tobacco or nicotine may be unfamiliar and act as a deterrent. TRP flavours that youth recognize from foods or candy can, however, increase their inclination to try TRP and reduce their perceptions of harm *(43,44)*. When a CYA tries a TRP, the flavouring compounds can mask the inherently aversive sensations produced by tobacco, nicotine or by-products of aerosolization or smoking, such as bitterness, irritation/burning sensations and thermoreceptor activation from high temperature. Additionally, flavourings themselves can be perceived as enjoyable and elicit sensations that CYA like, such as sweetness, fruit, mint and coolness. By altering the user experience, flavourings in TRP remove factors that tend to deter young people from continuing use of a product after an initial trial and promote desirable experiences that encourage persistent use. Flavours in TRP substantially increase their appeal for various demographic groups, although the extent of appeal-enhancement by flavours may differ among groups because of heterogeneity in user experience and targeting of industry marketing towards specific populations.

Many flavoured TRP are marketed with product names that are explicitly aligned with the sensations the product will elicit (e.g. cherry, blue raspberry, peppermint). Other flavoured TRP are marketed under names that are ambiguous with respect to flavouring, often in settings where flavoured TRP are restricted. For example, the nicotine pouch brand Zyn changed the names of flavours in its products from "mint" to "cool" after certain US states banned mint-flavoured TRP. Some products are marketed as "tobacco flavoured" or "unflavoured" but contain flavouring chemical additives. "Non-menthol" cigarettes and "clear" e-cigarettes, which may lack noticeable flavouring additives other than a synthetic non-menthol coolant, have been marketed as "unflavoured", especially in regions where flavoured tobacco has been banned. TRP with synthetic coolants have, however, been shown to have similar appeal to those with menthol and are therefore considered by certain regulatory agencies to be flavoured or to contain banned additives.

2.3.2.2 Non-flavour additives or other modifications that increase sensory appeal

In TRP with high pH, the nicotine is in its free-base chemical state, which is inherently perceived as bitter and irritating to the airways and oral cavity. By including organic acid additives or by other manufacturing processes (e.g. curing), the pH of a TRP is lowered and the nicotine protonates into a salt form, which is perceived as less bitter and harsh than free-base nicotine. As bitterness and harshness are deterrents, especially to CYA, TRP with acid additives and low pH may be disproportionately used more by CYA than by other age groups.

As well as additives, manual modifications to TRP can reduce their irritation and harshness. Such modifications include placing filters on cigarettes or cigars, increasing ventilation on cigarette filters and modifying the airflow to e-cigarettes. Each of these modifications can affect the concentrations of acrolein, free-base nicotine and other sensory-irritant compounds in smoke and aerosol by diluting it with air. These modifications thus make TRP less aversive to CYA.

2.3.2.3 Design for discreet use and concealability

CYA report that the ability to conceal use of certain TRP from parents, peers and other authority figures (e.g. teachers, employers) is one of the key reasons for using them. Many new and emerging products are designed to be used discreetly. For example, some e-cigarette devices resemble everyday items such as USB drive pens, highlighters, cosmetic products and watches. Some "hoodies" have built-in e-cigarette mechanisms *(45)*. Most smoked products emit tobacco smoke with an odour, which persists on the user's clothing and hair long after use and remains detectable. E-cigarettes and oral TRP do not produce odours that smell like tobacco smoke and can be used immediately before meeting parents, employers and other authority figures from whom CYA may wish to hide their TRP use. Some e-cigarette products are designed to emit less visible aerosol when exhaled, and some devices even have specialized settings (e.g. "stealth mode") that modify the heating mechanism to emit less visible aerosol *(46,47)*. Because of such design modifications and their diminutive design, CYA have been reported to use e-cigarettes in places where they are prohibited, such as at school, at work or on public transport or airplanes *(46)*.

Newer products, such as nicotine pouches and other oral nicotine products, do not require the user to spit during use, and the sachet is disposed of after use. TRP marketing strategies claim that these products can be used directly in the presence of authority figures, such as by placing the product between the cheek and gums. Nicotine gums, gummies, lozenges, mints and hard candy can be used in the presence of authority figures because they are indistinguishable from non-nicotine chewing-gum and candy *(48)*.

2.3.2.4 Convenience and low cost

The time, effort, preparation and cost of TRP may deter CYA from TRP uptake. The convenience of use of different TRP classes and product types varies widely. Roll-your-own, pipe tobacco and other loose tobacco products that require the user to prepare portions of TRP before use may be perceived as inconvenient and disincentivize use by CYA *(49,50)*. Commercial cigarettes and other smoked tobacco products and brands that are pre-rolled are substantially more convenient, usually less costly, and disproportionately used by CYA rather than roll-your own products or pipes. Products that require several components or supplementary accessories for use, including smoked tobacco products that require a lighter, are less convenient than more recent single-component products that can be used alone (e.g. disposable e-cigarettes). Not all newly-introduced TRP are single-component; for example, use of HTP may require both a heating device and sticks with specially processed tobacco or supplementary accessories. There is wide variation in convenience, ease and cost within product classes. In the e-cigarette class, rechargeable devices with refillable tanks are less convenient, more expensive and less commonly used by CYA in various European and North American countries than disposable pre-filled e-cigarette devices *(51–53)*. Disposable devices, often sold at lower prices, reduce the barriers for CYA. Increasing the price of tobacco products through taxation has consistently been shown to discourage tobacco uptake by CYA *(54,55)*.

2.3.2.5 Product design that attracts CYA by resembling CYA-oriented products (including food and toys)

Flavoured TRP are marketed with the names of candy and appealing imagery, often resembling non-nicotine products, which may appeal to CYA (see Table 2.1) *(48,56)*. Some hookah, pipe and e-cigarette products are designed to resemble non-TRP, such as sweet beverages, water bottles, toys and other common items (e.g. digital watches). Furthermore, recent e-cigarette products resemble video games and have interactive screens on which the user can play. The entire class of non-medicinal nicotine gums, gummies, lozenges, hard candy and mints cannot be differentiated from their non-nicotine counterparts, especially in the absence of labelling standards that would require manufacturers to clearly indicate on each item that the product contains nicotine *(48)*.

2.3.2.6 Unique CYA appeal of nicotine products, synthesized nicotine and nicotine analogue products

Through successful public health messaging, tobacco products have increasingly become perceived by CYA as unappealing, socially undesirable and harmful. In the 21st century, commercial TRP have been introduced that are claimed not to

contain tobacco leaf, shredded, ground, cut or in any other solid form, while they do contain nicotine or nicotine-like psychoactive substances. When TRP labelled as "not containing tobacco", such as e-cigarettes, were first introduced, they were marketed as products intended for adults who smoke and resembled their tobacco-containing versions *(57)*. Over time, the design and marketing of these products distanced them from smoked cigarettes, creating the perception that they did not have the harm and social undesirability of tobacco-containing products such as cigarettes *(57)*. Recent nicotine products, such as nicotine pouches, are marketed in such a way as to distance them from tobacco products. Consequently, much public health education that has changed the perception of the harm of tobacco products does not cover new products such as e-cigarettes, which might account, in part, for increased use of such TRP in some regions.

Some e-cigarette and nicotine product manufacturers have used synthesized nicotine rather than tobacco-derived nicotine and claimed that synthesized nicotine is "cleaner" and less toxic than that derived from tobacco, despite the absence of any scientific evidence to substantiate such claims *(58,59)*. Recently, e-cigarettes and products containing nicotine analogues have emerged, which may not be subject to certain TRP regulations in countries that do not consider or include them in their definition of nicotine or tobacco products (see Table 2.1). These products do not contain nicotine per se but contain analogues that have a similar chemical structure to nicotine (e.g. 6-methyl-nicotine) and may have similar pharmacological activity. The manufacturers of these products also market nicotine analogue e-cigarettes and pouches as being "cleaner" and providing a nicotine-like experience without tobacco toxicants, another claim that has not been independently scientifically substantiated.

2.3.3 Abuse liability of tobacco and related products

"Abuse liability" refers to the extent to which the design, constituents and to some extent the marketing of TRP increases the probability that a person who initiates use will develop patterns of use and symptoms indicative of addiction (Fig. 2.1). "Addiction" refers to compulsive, frequent use of a TRP, craving, distressing withdrawal symptoms upon discontinuation, difficulty in quitting and continued use despite experiencing negative social, psychological or physiological consequences of use *(60)*. Consideration of abuse liability is vital in the case of CYA, because the developing brain is more vulnerable to addiction. Hence, the effect of TRP abuse liability on addiction and the negative consequences of chronic TRP use may be amplified in CYA. The principles of abuse liability can be generalized to many cultural contexts and are therefore relevant globally. In addition to sensory cues, such as "throat hit" and behaviours, such as hand-to-mouth actions, some other factors that influence abuse liability are outlined below.

2.3.3.1 Nicotine concentration

Nicotine is the principal addictive agent in virtually all TRP. TRP classes differ in the concentration of nicotine in the product and, in turn, the amount of nicotine delivered to the user. The concentration of nicotine in a product is generally proportional to its abuse liability, if it does not exceed a threshold of toxicity, although various factors can moderate the relation between nicotine concentration and abuse liability (see below). There is a concentration below which nicotine is not addictive, although this differs among products, depending on factors such as route of administration, rate of absorption and delivery and the concentration of nicotine in the product. The nicotine concentration in many tobacco-containing products differs according to the plant type or whether the plant is genetically engineered and how it is grown and processed, as well as varies with jurisdiction due to permitted maximum limits. For example, the nicotine yield per conventional cigarette can range from 0.1 mg/cigarette to upwards of 2.7 mg/cigarette by brand. E-cigarette solutions can contain as little as 0.2% nicotine or from ~2 mg/mL nicotine to > 6% or 60 mg/mL. The nicotine concentration in nicotine pouches can vary from 1 to ≥ 30 mg per portion *(61)*.

2.3.3.2 Method of administration

The speed at which an addictive compound such as nicotine is delivered through the bloodstream is generally proportional to its abuse liability *(62)*. Hence, inhaled products that deliver nicotine into the bloodstream via the pulmonary route through boluses of nicotine extracted from each puff are associated with the greatest abuse liability. This mode of delivery is that of many inhaled TRP that emit nicotine-rich smoke (e.g. cigarettes) and for inhaled TRP that emit nicotine-rich aerosol (e.g. e-cigarettes, HTP). Ingestion and transdermal administration are associated with the lowest abuse liability. Oral tobacco, nicotine and related products (such as snus, snuff, nicotine pouches) that users place between the cheek and gums come into contact with buccal blood vessels, which results in slower nicotine absorption than from inhaled products, although they still deliver substantial nicotine and, therefore, have significant abuse liability *(62,63)*.

2.3.3.3 Additives and manufacturing processes that change pH or enhance nicotine absorption

Manufacturing processes and additives that lower pH or otherwise protonate nicotine offset the aversive sensory properties of high nicotine concentrations, with synergistic increases in abuse liability for young people *(64)*. Lower pH allows users to inhale the product more deeply, which in turn increases the amount of nicotine delivered to the bloodstream *(64,65)*. Similarly, products with lower pH may reduce burning sensations, so that users keep them in contact with buccal

blood vessels for longer, also resulting in delivery of more nicotine *(66)*. Certain TRP with a high pH that are tolerated by users result in greater absorption of freebase nicotine in the buccal cavity *(67)*. Additives such as ammonia facilitate nicotine uptake and absorption.

2.3.3.4 Flavours and other sensory enhancers

Flavours and other sensory-enhancing additives increase abuse liability by increasing inhalation of TRP products, allowing deeper puffs and more nicotine delivery *(68)*. Additionally, the reward-enhancing effects of nicotine add to pleasant sensory stimuli to enhance the addictiveness of TRP *(69)*, which also contributes to the abuse liability of TRP with flavours and other sensory enhancers.

2.3.3.5 Nicotine analogues and other non-nicotine psychoactive compounds

E-cigarettes and nicotine products containing nicotine analogues, such as 6-methyl nicotine, have been shown to have similar (and in some cases more) pharmacological activity at nicotine receptors *(70)*. Preclinical research in experimental animals indicates that some nicotine analogues and nicotine elicit similar increases in motor activity *(70)*, which is a marker of the psychostimulant effects of the drug and is often correlated with abuse lability. While clear data on the abuse liability of these products are lacking, the evidence suggests that TRP with such analogues may be psychoactive and addictive. Additionally, various TRP, including cigarettes, have been shown to contain monoamine oxidase inhibitors that combine or synergize with nicotine to increase their addiction potential *(71–73)*. Furthermore, menthol has been shown to have central nervous system effects on nicotine acetylcholinergic receptors, independent of its sensory-modifying effects *(74)and menthol cigarette smokers tend to upregulate β2* nAChRs more than nonmenthol cigarette smokers. We investigated the effect of long-term menthol alone on midbrain neurons containing nAChRs. In midbrain dopaminergic (DA*. Overall, non-nicotine compounds in TRP that have central nervous system activity might contribute to their abuse liability and the risk of CYA for addiction.

2.3.3.6 Device power

The power of an e-cigarette device modifies the density of the aerosol consumed and in turn the constituents in the e-cigarette solution, including nicotine and other toxicants *(75)*. Even in liquids with a lower nicotine concentration, high vs lower wattage increases measures of abuse liability *(76)*, as it can result in delivery of more nicotine to the user and impact the sensory profile, including making the product less palatable at higher nicotine doses unless flavours are present to mask this effect *(77)*. People who use devices in which the user can modify the voltage report greater nicotine dependence *(78)*. Therefore, power settings should be addressed, in addition to other measures, such as nicotine concentration, to reduce the abuse liability of TRP.

2.3.4 Impact of TRP marketing on use by CYA

The TRP industry has a long history of aggressive, sophisticated targeting of youth and young adults in its marketing to recruit new consumers *(79–81)*, which has been successful in driving tobacco and nicotine use among CYA *(79–82)*. Extensive evidence from various geographical locations, with different methods and in different disciplines demonstrates a strong, consistent causal effect of tobacco marketing and promotion on positive perceptions of tobacco and nicotine use and increased rates of initiation and progression to heavy use among CYA *(79,81)*. Portrayal of TRP use as desirable, rebellious or sexy by celebrities, influencers and other admired figures in advertisements normalizes and glamourizes the behaviour in a way that especially attracts CYA *(81)*. Additionally, the design of packaging to make TRP resemble non-TRP with which CYA are familiar (e.g. candies) can affect their perceptions and use.

Today's marketplace of tobacco, nicotine and related products includes both conventional smoked tobacco products such as cigarettes and newer products such as e-cigarettes and nicotine pouches. Further, entertainment platforms have developed beyond traditional television and radio broadcasts to include new digital media, such as social media, online video games, streaming services and podcasts on which TRP can be promoted.

Social media use by CYA is widespread and has increased significantly in recent years *(83,84)*. In the USA, 93% of adolescents use social media and spend an average of 5 h/day on such platforms *(85,86)*. Globally, 36% of adolescents use social media, and 1 in 10 show signs of problematic social media use *(87)*. Because they are heavy users of these media, CYA are often targeted by marketing campaigns and are highly susceptible to carefully crafted themes and visuals that portray tobacco use as aspirational, glamorous, cool, celebratory, exotic, rebellious and socially normative *(79,81,82)* (See Table 1 for some examples of youth-appealing tobacco marketing content on social media.) Such marketing campaigns feature youth-appealing tobacco, nicotine and related product characteristics such as fruit, candy, dessert and concept flavours. While traditional paid advertising is still used, social media and other new media enable more organic strategies, such as influencer promotion, which appears to be more "authentic", to ensure high levels of engagement with viewers. These strategies push the boundaries of what is normative, often without some young people realizing that they are being targeted.

CYA around the globe report seeing TRP advertising and engaging with social media content *(88–93)*. Emerging data show that both exposure to and engagement with tobacco, nicotine and related content on social media significantly impact the perceptions and behaviour of CYA *(91,94–96)*. One study showed that daily use of a specific social media platform was associated with a 3.8% increase in risk for current e-cigarette use by middle-school students and a 6.1% increase among high-school students *(97)*. Another study found that each

additional hour per day spent on such platforms by first-year university students was associated with a 4.6% increase in the probability of lifetime e-cigarette use *(98)*. Even brief exposure to e-cigarette content on social media was associated with greater intention to use these products and more positive attitudes toward e-cigarettes *(99)*.

Although CYA spend a substantial time in the digital space, they are also exposed to tobacco and nicotine marketing in the physical space. The tobacco and nicotine industries continue to promote their products and brands to young people in physical locations by sponsoring sports events, concerts and festivals and by advertisements at retailer points of sale, product packaging and strategies such as direct mail campaigns. Brown et al. *(100)* observed that, in 42 primarily lower–middle-income countries, point-of-sale cigarette advertisements were common in retailers near schools and playgrounds. Cigarette packs and single sticks of cigarettes were displayed near snacks and sweet drinks. Cigarette advertisements featuring flavoured cigarettes were often placed at children's eye level. As of 31 December 2024, at least 122 countries had prohibited advertising of tobacco products at points of sale, and 59 prohibited display of tobacco products at points of sale *(11)*.

2.4 Prioritization of protection of children and young people

2.4.1 Tools

Monitoring, surveillance and regulations are vital tools for reducing CYA use of TRP. Application of these tools varies widely among countries. As of 2025, 183 countries, including the European Union, representing more than 90% of the world's population, had ratified the WHO FCTC *(101)*. Of the Parties that ratified the WHO FCTC, a variable percentage reported having adopted some form of policy or regulation in 2022–2023. It is not known how many countries actively regulate the manufacture and marketing of products with nicotine analogues and the specific regulations that are applied.

The WHO MPOWER package *(102)* is a comprehensive set of measures intended to assist countries in implementing effective interventions described in the WHO FCTC to reduce the demand for tobacco. The six measures are: Monitor tobacco use and prevention policies; Protect people from tobacco smoke; Offer help to quit tobacco use; Warn about the dangers of tobacco; Enforce bans on tobacco advertising, promotion and sponsorship; and Raise taxes on tobacco. In 2024, more than 6.1 billion people (over 75% of the world's population) were covered by at least one MPOWER measure that addressed one or more TRP, which was implemented at the highest level. Forty countries, however, had not yet adopted a single MPOWER measure at best-practice level, leaving almost 2 billion people, including millions of CYA, vulnerable to the harms of tobacco *(11)*. Additionally, many countries that have adopted MPOWER practices have

done so for only a limited subset of TRP classes (e.g. cigarettes only, tobacco-containing products only). Although some countries have extended such measures to nicotine and related products, for many products, there is still no effective control measure or regulation in many parts of the globe. As of 2024, 48 countries banned or regulated nicotine pouches, including 16 countries that banned their sale. Of the 133 countries that regulate e-cigarettes in some way, 42 (representing 2.7 billion people) ban their sale, and the other 91 countries have adopted (completely or partially) one or more legislative measure to regulate e-cigarettes. For HTP, 102 countries specifically regulate them, including 24 countries that ban their sale *(11)*.

2.4.2 Surveillance

To prioritize protection of CYA, continuous, timely surveillance of trends in perceptions and use of tobacco and nicotine, including marketing and sales practices, is essential. Many countries, however, do not monitor TRP use by CYA or do not assess use of specific TRP or dual or poly use. A multi-modal surveillance system with various data collection streams is described below, by mode of surveillance. As each mode of surveillance has unique strengths and weaknesses, multi-model systems are useful for triangulating many information sources to ensure comprehensive monitoring.

2.4.2.1 Surveys

Population-based surveys with random probability sampling of CYA in a country provide the most robust estimates of the prevalence and patterns (e.g. frequency) of use and of perceptions. School-based surveys, in which large groups of CYA are sampled in schools, and household surveys, in which exhaustive listings of residents are used to select households, can be used to obtain representative estimates of use. School-based surveys with self-administered questionnaires are less resource-intensive than surveys administered in households by interviewers and may provide more precise estimates, as youth may be reluctant to report TRP use to adults in the presence of their caregivers *(103)*. Data should be collected on various product categories, including multi-product use, to assess the patterns, frequency and drivers of use in different population groups and to inform targeted interventions and regulatory responses.

2.4.2.2 Observations and sales in "brick-and-mortar" stores

To identify the products most widely marketed and sold, direct observation in "brick-and-mortar" retailers (i.e. shops that sell products directly to consumers and not via the Internet) is useful *(104,105)*. Visits to such shops can provide information on marketing approaches (e.g. at the point of sale, promotions) and whether restrictions on minimum age purchase are being enforced. Standard assessments

are available for such visits *(104,105)*. Systematic, representative canvassing of the retail market in an entire country can be resource-intensive and difficult.

Some third-party companies track and collate reasonably comprehensive data on sales of TRP in retailer outlets in some countries *(106)*; however, the data do not include every type of retailer (e.g. e-cigarette shops) or the age of purchasers or sales to youth. Such surveys can also be costly *(106)*.

2.4.2.3 Surveillance of retailers on the Internet

Systematic observation of the websites of TRP manufacturers, retailers, wholesalers and distributors can be useful for collecting information on TRP products sold on the Internet *(107)*. Tabulation of the products sold and identification of marketing materials and consumer reviews on TRP retail websites can indicate probable exposure of CYA to TRP. Additionally, Internet surveillance of TRP retailers can provide information on age gating, whether young people who are below the legal age for purchasing TRP in a country can purchase products without robust verification of age. Internet surveillance of retailers can be cost-efficient but difficult to do systematically in view of the vast number of Internet retailers.

2.4.2.4 CYA advocates and advisory groups

Youth advocates or advisory groups can be created to collaborate with surveillance groups and regulators to rapidly obtain detailed information on emerging trends in TRP use patterns and marketing approaches targeting CYA. This involves recruiting trusted members of the target CYA community, who have used TRP or are in social networks with CYA who use TRP. Through dialogue, youth advocates become skilled at identifying new trends in TRP use and marketing that are of interest to surveillance specialists and regulators, and the advocates and surveillance specialists learn together *(108)this article 3*. By involving CYA as active stakeholders, this method not only extends their perspectives but equips them with skills for advocating for meaningful policy changes. Their participation both provides information and empowers them to contribute to the development of and advocacy for tobacco policy by collaborating with researchers, thus ensuring that their voices and experiences are represented *(109–111)*. As CYA are directly targeted by the tobacco and nicotine industries and bear the consequential health effects of using tobacco, nicotine and related products in the long term, their involvement can drive policy change *(110,111)*.

2.4.2.5 Surveillance of social media

Social media platforms make it possible to conduct surveillance of TRP industry's marketing and sales practices (e.g. by paid influencers) and of the general public's perceptions of TRP. The information can provide early information on trends in use of new products and features of products that appeal to CYA that could

be regulated. Social media serve as a "digital town square", where individuals freely express and discuss their thoughts and opinions, providing information on their perceptions and reactions about tobacco products *(112)*. Systematic, timely collection and analysis of the content of relevant posts is useful for monitoring content on tobacco and nicotine on social media. The content can be searched through hashtags and keywords with various tools and data sources, such as the social media application program interface, which allows researchers and developers to access and analyse public data, third-party software (e.g. Netlytic) and customized "web scrapers" for systematic collection and analysis of the content of relevant posts, including text, images, videos and geolocation *(113,114)*.

Social media content, including images, text, videos and comments, can be analysed qualitatively by hand or with automated machine learning techniques, which can complement and supplement hand-coding *(115,116)*. While social media surveillance is useful and can be conducted at modest cost, it is difficult to determine whether social media posts are accessed by CYA or by other age groups, as the age of users is considered to be private information. Ethical concern arises about user privacy, informed consent and use of publicly available data for research without clear guidelines. A threat to data quality is the tendency of social media to be skewed towards extreme opinions, which may not accurately represent the attitudes of the general population *(117)*, Social bots, automated programs designed to simulate human behaviour, exacerbate bias on social media *(112,118)*. In the context of tobacco, nicotine and related content, they often promote pro-tobacco and pro-nicotine messages *(112)*, which can complicate identification of posts that reflect actual public opinions. This concern indicates that a framework should be formulated to establish best practices for ensuring reproducibility and replicability in monitoring and analysing tobacco content on social media *(113,114,119,120)* and indicate the utility of using multi-modal surveillance systems rather than only one.

2.4.3 Regulation of TRP to protect CYA

2.4.3.1 Overview and regulatory mechanisms

The regulatory policies and mechanisms used to protect CYA from TRP use differ by country and by product. The mechanism may be a law, a decree, a resolution, a circular, a notification or an amendment to legislation. Various regulatory approaches have been used for TRP, usually as consumer products, and with certain products being regulated as pharmaceutical drugs, such as in Australia. Countries differ in whether they require regulatory review before legal marketing of a TRP. If a pre-market regulatory review is required, countries differ in enforcement of policies and whether they include specific protection of CYA. Selected regulatory policies are reviewed below, mainly those on newer, emerging nicotine and tobacco products that may appeal especially to CYA, including e-cigarettes, nicotine pouches and HTP.

The estimates of the numbers of countries that have adopted specific policies are derived from the "litigation tracker" of the Campaign for Tobacco Free Kids *(121)*, the Johns Hopkins Global Tobacco Control Policy Scan *(122)* and the WHO report on the global tobacco epidemic *(11)* and technical notes.

2.4.3.2 Comprehensive ban on manufacture and sale to CYA of all TRP or all TRP in a specific product class

Several countries temporarily banned sales of TRP during the coronavirus disease 2019 (COVID-19) pandemic. For example, 17 countries in the Eastern Mediterranean Region prohibited use of waterpipes (*shishas*) in public places, and South Africa temporarily banned tobacco sales as part of a broader restriction on "non-essential" products during its pandemic response *(123)*. Some localities have since enacted such bans, the most common application of this policy being a ban on sales but not on manufacture *(124)*.

Some countries have proposed a ban on tobacco products for anyone born after a certain date, with the aim of creating a "smoke-free generation" [1] *(125)*. Several cities in Massachusetts, USA, have such policies. The most recent to do so, Newton, banned the sale of tobacco to anyone born on or after 1 March 2004 *(126)*. Several other states in the USA, including Hawaii and Indiana, have proposed similar policies. In Hawaii, Senate Bill 429 proposed that, from 1 January 2026, it will be unlawful to sell or provide any tobacco product, in any form, or any electronic device for TRP to an individual born on or after 1 January 2005. Similarly, Indiana introduced Senate Bill 322, which makes it an offense to sell tobacco products, e-liquids or electronic cigarettes to individuals born after 30 June 2004 *(127,128)*. The aim of these age bans is to prevent CYA from initiating use of any tobacco product, thereby safeguarding them from addiction and the potential health risks associated with tobacco use. The United Kingdom announced a proposal and is in the legislative process (as of October 2025) to make it an offence to sell tobacco products, herbal smoking products and cigarette papers to anyone born on or after 1 January 2009. The tobacco products include cigarettes, hand-rolled tobacco, cigars, cigarillos, pipe tobacco, waterpipe tobacco, chewing tobacco, heated tobacco and nasal tobacco *(129,130)*. The United Kingdom Department of Health and Social Care projected that implementation of the policy would significantly reduce the prevalence of smoking among individuals aged 14–30 in England. Within 3–10 years of enactment, the smoking rates in this age group could decrease to half of current levels, potentially approaching zero by 2040 *(25)*. New Zealand, however, which initially adopted a generational tobacco ban, reversed the policy under its new government, citing concern about potential loss of tax revenue and the risk of increased illicit trade *(131)*.

1 Maldives has become the first country in the world to introduce a generational tobacco ban, which came into effect on 1 November 2025. The law prohibits the sale and use of tobacco for anyone born after 1 January 2007.

The more common regulatory intervention is a ban on sales of specific product classes. For two TRP classes that especially appeal to CYA – e-cigarettes and nicotine pouches – as of 31 December 2024, 42 countries had banned the sale of e-cigarettes, and 16 countries had banned the sale of nicotine pouches *(11)*. Such bans are in line with WHO FCTC Article 2.1, which encourages Parties to implement measures beyond those required by the Convention, and also with Article 5.2, which outlines Parties' obligations to develop appropriate policies for preventing and reducing nicotine addiction.

2.4.3.3 Minimum age purchase laws

Most countries require a minimum age for purchasing cigarettes, varying from 16 to 21 years. Minimum age purchase laws are less commonly applied for new and emerging tobacco, nicotine and related products that may appeal to CYA, such as e-cigarettes, nicotine pouches and HTP, than for smoked products. In 2024, there was no minimum age at which e-cigarettes could be bought in 74 countries, covering a population of 1.9 billion people *(11)*. Thus, nearly 50% of countries that allow the sale of e-cigarettes restrict sale to minors, although 90% of countries apply age restrictions to cigarette purchase *(11)*. As of December 2024, fewer countries applied laws on the minimum age for purchasing HTP (74 countries) and nicotine pouches (26 countries) *(11)*. It has been proposed that a higher minimum age (e.g. ≥ 21 years) would be more effective in restricting CYA access *(132)*. It should be noted that the rapid growth of Internet sales has created new means for circumventing age restrictions, as laws for verifying age in online transactions are often weak or easily bypassed.

2.4.3.4 Restrictions on sales to CYA of TRP with specific product characteristics or design features that attract CYA

Regulations based on the presence of certain constituents, their levels and design features have been adopted by some countries for some TRP classes. Regulation rather than imposing a ban may include measures to prevent appeal and addiction, in line with Article 5 (2b) of the WHO FCTC. It may also prohibit or restrict ingredients that are likely to increase the palatability of products (such as flavours), as recommended in the Partial Guidelines on Articles 9 and 10 of the WHO FCTC *(133, 134)*, in order to reduce uptake by CYA or by never users.

- **Flavours**. Flavour bans are either comprehensive, covering all flavours (other than tobacco), or partial, for specific flavours or product types. They usually restrict a flavouring additive but may extend to use of flavour terms in marketing. The European Union Tobacco Products Directive *(135)* bans flavoured cigarettes and HTP, and a few agencies either fully ban all non-tobacco flavours or impose partial bans that

exempt menthol. Restrictions on flavours in HTP have been imposed by 29 countries partially, on specific flavourings but not on all non-tobacco flavours (e.g. New Zealand exempts tobacco, mint and menthol flavours). In 15 countries that permit the sale of e-cigarettes, there is a partial ban, or specific flavours are permitted; 7 countries ban all non-tobacco flavours *(11)*. In the few countries that regulate sales of nicotine pouches, Canada, Denmark and Finland restrict some flavours *(136–138)*.

- **Other additives that facilitate nicotine uptake**. With respect to the inclusion of additives to TRP, some countries prohibit sugars or other ingredients that facilitate nicotine uptake (e.g. ammonia) or nicotine absorption or make products easier to inhale, in alignment with Articles 5.2 and 9 of the WHO FCTC. Policies in several countries call for a ban on all cooling agents, including those that are flavourless or odourless, and acid additives that reduce the bitterness and harshness of TRP, including e-cigarettes, nicotine pouches and other products *(134)*.
- **Nicotine additives and their concentrations**. Several countries, such as Denmark, Finland and Ukraine, limit addition of nicotine on the filter and casing of smoked tobacco products or in capsules. At least 51 of 88 countries and jurisdictions that regulate e-cigarettes, cap the maximum nicotine concentration in e-liquids, such as 20 mg/mL in the European Union Tobacco Products Directive in 2023 *(135,139)*. The ninth report of the WHO Study Group on Tobacco Product Regulation *(134)* recommended that, in countries in which the sale of nicotine pouches is permitted, an upper limit on nicotine be set to reduce the addictiveness and harm of the product. The Study Group in its seventh report *(140)* recommended that a reduction in the concentration of nicotine to ≤ 0.4 mg/g would benefit the largest population of current and potential smokers. Many countries have set a limit on the nicotine concentration in tobacco products, particularly cigarettes. Many have set a limit of 1 mg per cigarette, while the Gulf Cooperation Council has set a maximum limit of 0.6 mg of nicotine per cigarette to reduce the addictiveness of the products *(141)*. In 2022, New Zealand mandated that an individual smoked tobacco product contain no more than 0.8 mg/g of nicotine, in an attempt to "denicotinize" tobacco; however, the Act was repealed after a change of government *(142,143)*. The US Food and Drug Administration has proposed that the level of nicotine be 0.7 mg/g of tobacco in cigarettes and certain other combusted tobacco products, to reduce the addictiveness of the products, and the proposal is being made into law *(144)*.

- **Synthetic nicotine and nicotine analogues.** Countries that have updated their tobacco product regulatory policies to address synthetic nicotine include Brazil, Kazakhstan, Thailand and the USA. Manufacturers are, however, including non-nicotine tobacco alkaloids or synthetic nicotine analogues in TRP, thus bypassing regulations that address nicotine alone. In New Zealand, the regulations prohibit the sale of cigarettes containing any synthetic or naturally occurring chemical or ingredient similar to nicotine or synthetic nicotine, and the state of California in the USA regulates nicotine analogues in the same way, with the same policies as applied to nicotine in TRP.
- **Designs to promote discreet use or convenience or resemble youth-appealing foods, toys and other non-TRP objects that appeal to CYA.** In Belgium, France, Ireland and the United Kingdom, a ban has been proposed on single-use disposable e-cigarettes, which are small, can be used discreetly and are convenient for CYA. Australia has banned domestic manufacture, commercial possession and sale of non-therapeutic e-cigarettes and disposable e-cigarettes since 1 July 2024 *(145)*, and New Zealand has passed a similar law, banning the distribution, manufacture, sale and supply of disposable e-cigarette devices, which came into effect on 17 June 2025 *(146)*. The USA has prioritized enforcement of unlawful sales of small, pod-style e-cigarettes. New Zealand bans the sale of TRP that resemble toys or cartoon characters *(147)*, and the USA prioritizes enforcement of laws to prohibit the sale of e-cigarette that resemble youth-appealing characters, toys, candy or school supplies *(148)*. The United Kingdom has proposed a similar ban, which was being considered in the UK Parliament as of October 2025 *(149)*.

  In several countries, products that resemble tobacco products are also banned. Türkiye has banned chewing gum, candies, treats, toys, clothes, jewellery, accessories and similar products that resemble tobacco products or tobacco brands *(150)*. Similarly, Singapore has banned any confectionery or other food product or any toy, device or article that resembles tobacco products or can be smoked or that may be used in such a way as to mimic the act of smoking or the packaging of which resembles, or is designed to resemble, the packaging commonly associated with tobacco products *(151)*. Brazil also bans the manufacture, import, sale, distribution and advertising of products of any nature and their packaging intended for children and adolescents that resemble the shape of cigarettes or similar products *(152)*.

2.4.3.5 Marketing, packaging and advertising of TRP

Regulations on the marketing, packaging and advertising of TRP have been adopted by some countries.

- **Advertising and promotion**. Article 13 of the WHO FCTC mandates comprehensive bans on all forms of tobacco advertising, promotion and sponsorship, in alignment with each country's legal and constitutional authority *(153)*. The restrictions encompass both direct and indirect advertising in all traditional media (e.g. print, television, radio) and newer digital media (e.g. social media, mobile phones, streaming services). Notably, Article 13 goes beyond traditional paid advertisements to encompass surrogate advertising and broader forms of tobacco promotion. These include practices such as product placement in an entertainment content (e.g. films, television shows, music videos), tobacco packaging with appealing colours or designs, corporate sponsorship of cultural and sports events, marketing of accessories linked to tobacco and nicotine use and promotional display of tobacco, nicotine and related products at points of sale. This WHO FCTC recommendation is reiterated in COP Decision FCTC/COP10(23) *(8)*. Implementation of marketing regulations differs significantly, however, among countries *(154,155)*, as only 68 countries ban tobacco advertising, promotion and sponsorship at best-practice level. More than 100 countries restrict the advertising, promotion and sponsorship of e-cigarettes *(11)*. Australia, Norway and the United Kingdom have banned all forms of tobacco advertising, while Indonesia, the Republic of Korea and the USA maintain partial bans.
- **Plain packaging and product requirements**. Plain packaging is an effective intervention for reducing the appeal of tobacco, nicotine and related products, as it consists of removing branding elements such as logos, colours and designs on cases and on the products themselves *(156,157)*. Tobacco, nicotine and related products are instead sold in uniform packaging, with standardized colours, sizes and fonts, without the company logo or colours and with prominent health warnings, reducing their attractiveness *(158)*. Evidence from Australia, which was the first country to implement a plain packaging policy, suggests that plain packaging reduces the prevalence of smoking among CYA and adults *(156)*. By the end of 2024, 25 countries had adopted plain packaging for cigarette packs, reducing the appeal and strengthening the impact of health warnings *(11)*.

2.4.3.6 Sales and pricing policies to limit access and affordability for CYA

As CYA are generally considered to be price-sensitive, regulations to reduce the accessibility and affordability of TRP are expected to help limit both initiation and continued use among this population.

- **Taxation.** High cost is a major deterrent for TRP uptake by CYA, and taxation policies that make products more expensive substantially reduce their TRP initiation *(159)*. Despite the impact of TRP taxes on use and recommendations in WHO FCTC Article 6, only 40 countries in 2024 applied tobacco taxes at or above 75% of the price of the most popular brand of cigarettes *(11)*. The taxation policies for other TRP are often different, taxes being lower or absent for HTP, e-cigarettes, nicotine pouches and other products *(160,161)*. As this often leads to exploitation, regulators should apply uniform taxes, as applicable, on all products.
- **Single-unit sales.** Sales of single units (e.g. single cigarettes) reduce the cost, thus removing the financial barrier to purchasing a full pack. Therefore, banning single-unit sales may act as a deterrent to many CYA, particularly in socioeconomically disadvantaged populations.
- **Maximum unit quantity per purchase (bulk sales)**. Bulk sales increase the likelihood of product diversion, whereby tobacco, nicotine and related products intended for adults are distributed to underage individuals. Limiting the quantity of products sold in a single transaction reduces opportunities for such redistribution and ensures stricter control over access. Single-unit and bulk sales can weaken the effect of increases in tobacco taxes by encouraging informal sales of single cigarettes *(162)*. This practice makes tobacco, nicotine and related products more accessible and affordable, particularly for CYA, by circumventing the price increases intended to deter use.
- **Internet and vending machine sales and restriction to sales in establishments with minimum age requirements for entry**. As of 31 December 2024, at least 118 countries banned vending machine sales of tobacco products, and 75 banned Internet sales of these products *(11)*. It is, however, difficult to enforce laws on minimum age purchase. Some jurisdictions have restricted sales to locations that require a minimum age to enter, such as bars and tobacco and nicotine specialty retailers.
- **Ban on sales at or near locations frequented by CYA.** Some countries have restricted TRP sales near schools and other educational facilities, playgrounds, stadiums, arenas, health-care facilities, cultural facilities, pharmacies, child-care centres and other establishments frequented by CYA.

2.4.3.7 Warning label requirements

Prominent displays of graphic and text warnings about the health risks of tobacco and nicotine can discourage initiation, promote cessation and educate CYA about their harmful consequences *(158,163,164)*. It has been reported that graphic warnings are impactful for CYA and that larger, more visually salient labels are often considered to affect risk perceptions and to deter use *(158,163)*. Countries differ in their rules and regulations on the size and placement of labels on packaging and on the text, which may alter their effectiveness in reducing CYA use.

The WHO FCTC recommends that Parties require health warnings and messages to appear on both the front and back (or all main faces) of each unit packet and package, specifically positioned on the principal display areas, preferably at the top to enhance visibility. It also advises that the warnings should cover at least 50% of the principal display area. Globally, 110 countries (with 5 billion people) now require graphic health warnings on cigarette packages, although only 54 countries require them on smokeless tobacco packages. Some countries have adopted even more stringent measures; for example, in 2022, Türkiye mandated that health warnings occupy at least 93% of the principal display area of cigarette packages. Australia and Canada have gone further by requiring health warnings on individual cigarette sticks. As of 31 December 2024, 56 countries required health warnings on the packaging (not restricted to graphic health warnings) of both devices and e-liquids. Three countries regulate health warnings on devices only and nine countries on e-liquids only *(11)*.

2.4.3.8 Banning use of TRP in public settings

Restrictions on the use of TRP in public places protect both CYA and adults who do not use them from the adverse effects of second-hand smoke. Children are particularly vulnerable to the harm of second-hand smoke, with increased risks of respiratory issues, middle-ear infections and sudden infant death syndrome. Smoke-free regulations can change the norm that TRP use is socially desirable and acceptable, which changes CYA perceptions of TRP and the risk of their use. Such policies have been adopted by many countries, although the range of public settings and products covered varies substantially by country. Some policies are restricted to smoked tobacco use, whereas others extend the policy to e-cigarettes or HTP, and a few extend it to smokeless tobacco. Additionally, the settings to which restrictions apply differ widely, from subsections of indoor settings (e.g. smoking zones, which are not protective and not recommended) to all indoor spaces or to outdoor public settings. The establishments that are subject to such policies also vary; they include government facilities, hospitals, child-care facilities, schools, public transit hotels and other settings. It has been shown that more comprehensive bans on use of TRP in public and those that cover a wide range of product categories are associated with lower rates of use by CYA *(116,165)*. As of 31

December 2024, 150 countries had adopted restrictions on smoking in educational facilities (excluding universities). In addition, 28 countries prohibited smoking in private vehicles in which there are children, and 66 countries had banned smoking in outdoor children's playgrounds and parks *(11)*.

2.4.4 Country case studies

2.4.4.1 Cigarettes in Australia

From early on, Australia adopted numerous tobacco regulatory policies for CYA that reduced cigarette smoking by this group, and it was the first country to pioneer plain packaging, in 2012 *(166–168)*. The policies included robust tobacco excise taxes, which have become stronger over time. Additionally, the ban on use of tobacco in public places has become more widespread and is among the most comprehensive, youth-focused bans in the world, as it includes smoking in automobiles in which there are children. Health warnings on tobacco packaging, bans on point-of-sale displays and other restrictions on advertising and promotion, plain packaging requirements and increased penalties for retailers for unlawful sale of tobacco to children have had a major impact. These policies, with strong public education programmes and regulations to reduce access of CYA to other TRP, including bans on smokeless tobacco and requiring e-cigarettes to be regulated and sold as a pharmaceutical product, have contributed to substantial decreases in smoking by Australian CYA. Among youth aged 12–17 years in a survey of Australian secondary school students, the rate of smoking in the past month had decreased from 24.8% in 1996 to 2.1% in 2022–2023 *(169)*.

Regulations on tobacco products were further tightened with the passage of the Public Health (Tobacco and Other Products) Act 2023 and the Public Health (Tobacco and Other Products) Regulations 2024. The regulations include requiring health warnings on certain individual cigarettes. E-cigarettes are further regulated through the Therapeutic Goods and Other Legislation Amendment (Vaping Reforms) Act 2024. The Act includes prohibition of the importation, domestic manufacture, supply, commercial possession and advertisement of disposable single use and non-therapeutic e-cigarettes. E-cigarettes are available in a pharmacy if they meet the Therapeutic Goods Administration regulatory requirements. Advertisement of e-cigarettes is banned in all media, including social media, as are other forms of advertising, promotion and sponsorship. Flavours in e-cigarettes are restricted to unflavoured, mint, menthol and tobacco.

2.4.4.2 E-cigarettes in the USA

The US national regulatory model does not place any ban or standard on the types of e-cigarette products that can be sold. Instead, individual manufacturers are required to submit applications for regulatory review to request legal marketing of their products, and decisions are made case by case. Before 2016, no minimum

age had been set for purchase of e-cigarettes, although several states had adopted local age restrictions.

E-cigarette design, marketing and manufacture evolved rapidly after their entry onto the US market in 2009. By 2019, an estimated 27.5% of US 14–18-year-olds reported current e-cigarette use, vastly exceeding the number of young people who used all other TRP. The availability of flavours, widespread marketing, sleek designs that facilitated discreet use and low cost have been the key drivers of e-cigarette use by CYA in the USA. From 2020, the country issued the following federal policies: (1) enforcing violations for illegal sales of unauthorized e-cigarettes with the mint or fruit flavours preferred by CYA in small pod-style designs that promote discreet use and appeal to CYA; (2) targeting of manufacturers of e-cigarettes resembling objects that appeal to youth, such as toys and video games, for enforcement and sending warning letters to cease sales; and (3) raising the minimum age to 21 years for purchase of all tobacco and nicotine products.

By 2024, 7.8% of US 14–18-year-olds reported current us of e-cigarettes, representing a 72% decrease in prevalence from the peak in 2019. Some of the decrease in e-cigarette use by CYA in the USA may have been due to the change in federal policy, with local policy changes, educational campaigns and other societal factors that influence use of e-cigarettes by CYA. Since 2018, the US Food and Drug Administration (FDA) campaign "The Real Cost" has prioritized public education to further reduce e-cigarette use by youth. The campaign has successfully changed perceptions of the risk associated with e-cigarette use. It offers targeted quitting resources for adolescents *(170)*.

Exemptions for menthol-flavoured e-cigarette products in US enforcement policies, uneven enforcement, no other regulatory tools and lack of comprehensive policies for regulating flavours in certain other TRP (e.g. nicotine pouches) may reduce the impact of US e-cigarette regulations. Addressing these limitations could reduce the prevalence of CYA use further.

2.4.4.3 E-cigarettes in the United Kingdom

E-cigarettes were initially regulated as consumer products and then, for a certain time, as medicinal products, until 2016, when they became subject to the assimilated rules of the European Tobacco Product Directive. These include limits on nicotine, including maximum nicotine concentration, bans on certain additives, ingredient labelling requirements, mandated health warnings and advertising restrictions. A minimum purchase age of 18 years was established in 2015 for e-cigarettes that contain nicotine. As of October 2025, no regulatory policies had been issued regarding flavours or product designs that appeal to CYA. However, relevant measures were under debate in Parliament as part of the Tobacco and Vapes Bill.

In this regulatory environment, the prevalence of current e-cigarette use by 16–17-year olds remained < 6% until 2018. Marketing restrictions, caps on

nicotine concentration and other regulations may have prevented widespread e-cigarette use in the United Kingdom until then, despite widespread e-cigarette sales. In the 4 years after 2018, however, current e-cigarette use by 16–17-year-olds more than doubled, to 14% in 2022–2024, and did not increase in the last three years *(171)*. Most e-cigarette use by CYA in the United Kingdom in recent years is of disposable e-cigarettes and flavoured products *(171)*. To address this trend, the Government has banned disposable e-cigarettes, effective from June 2025, and is considering restriction of flavours *(149,172)*.

2.5 Challenges and opportunities associated with comprehensive youth-focused tobacco control policies

2.5.1 Challenges to the adoption and effectiveness of TRP regulatory policies designed to protect CYA

2.5.1.1 Reluctance to introduce TRP policies

Policy-makers may be hesitant to introduce youth-focused policies because of concern about (1) intense lobbying by tobacco companies, related interests and tobacco-funded organizations; (2) potential impacts on business and the economy; (3) potential impact on adult smoked tobacco users' decision to switch to an allegedly "less harmful" nicotine and tobacco product by making more recent TRP less readily available and more costly; and (4) the resources required to operationalize and enforce such policies.

2.5.1.2 Compliance and enforcement

Suboptimal compliance with TRP regulatory policies undermines their impact. For example, the prevalence of TRP use in CYA living in areas in which vendors more often violate minimum age purchase policies is higher than in locations with the same policies but better local compliance *(173)*. Lack of retailer compliance with bans on flavoured TRP sales, marketing restrictions and other policies is a challenge. Enforcement activities, such as checks on retailer compliance, can be difficult to apply comprehensively because of the cost. Additionally, flavour bans can be complex to enforce, as some manufacturers market TRP with concept flavours, sweeteners and/or cooling agents. "Concept flavours" are ambiguously named flavours that do not necessarily correspond to the sensory experience of using them (e.g. a strawberry-flavoured constituent in an e-cigarette flavour called "Tigers Blood" or grape-flavoured additives in cigarillos labelled "Jazz") *(174,175)*. In addition, tobacco and nicotine products are often mislabeled. For example, of the waterpipe tobacco products notified to the European Union Common Entry Gate, 39% contained a menthol or mint flavour, and 83% contained one of more menthol-like ingredients when tested *(176)*. An additional challenge is introduction of flavour accessories that add flavour to otherwise unflavoured

tobacco products. The many flavouring accessories include capsules, cards, filter tips and tubes, drops, spray and rolling paper *(177)*. Therefore, a ban on flavoured TRP solely on the basis of products' names might miss concept-flavoured TRP that could appeal to CYA.

2.5.1.3 Rapidly evolving TRP market adapted to policies and policy loopholes

If a policy is not operationalized comprehensively, any ambiguity allows TRP manufacturers to adapt their products and marketing so that they comply with a policy but undermine the policy's impact on CYA. For example, the US regulatory framework for TRP initially defined a TRP as any product made of or derived from tobacco. Nicotine production was adapted to synthesis that does not require constituents extracted from tobacco. This resulted in mass manufacture of e-cigarettes and other TRP with synthetic nicotine, which were exempt from US regulatory TRP oversight. When the legislation was revised to include synthetic forms of nicotine, manufacturers subsequently created new TRP with nicotine analogue compounds that do not fit the legal definition of nicotine and are again not subject to enforcement. Similar challenges are presented by operationalization of flavour bans. Manufacturers adapted by adding synthetic cooling agents instead of menthol when policies banned certain flavours or included restricted or ambiguous definitions of flavours. Similarly, manufacturers of tobacco, nicotine and related products have increasingly shifted to digital advertising, including social media, to circumvent restrictions imposed in some countries on use of television, radio and print media. The shift is also driven by the rapid growth and influence of the Internet and social media platforms.

2.5.1.4 Challenges to prioritizing regulation of products for the greatest impact and to ensure equity

Some regulatory agencies have insufficient resources to develop and implement effective TRP regulations that address all products and all populations. In these cases, regulators might be tempted to address the products and populations that receive the most public attention, through media coverage of emerging products or the loud voices of majority groups. An unintended consequence can be to overlook disadvantaged populations who cannot afford newer TRP and use products that receive less attention by the media, including smoked cigarettes. Balancing regulatory priorities to ensure a maximal, equitable impact can be challenging, especially when resources are limited.

2.5.1.5 Concern that regulating products that appeal to CYA could limit switching attempts to newer TRP for adults who smoke

It is possible that regulatory restrictions on newer TRP that appeal to CYA could limit switching attempts for adults who smoke. For example, the Food and Drug

Administration, which is responsible for regulating most TRP in the USA, has cited this concern as the rationale for certain regulatory decisions to allow flavoured e-cigarettes and nicotine pouches on the market *(178,179)*.

2.5.2 Opportunities and methods for overcoming challenges to ensuring comprehensive, effective TRP regulatory policies that protect CYA

2.5.2.1 Stakeholder education about the benefits of youth-focused TRP regulatory policies and anticipated secondary impacts on adults

Policy-makers and other stakeholders may require information about the widespread health, social and economic impacts of youth-focused TRP policies. Modelling-based statistical analyses can project the impact of a policy on outcomes valued by stakeholders. Such information includes the estimated number of cases of preventable diseases avoided in a population, quantification of the projected economic benefits to employers because of less employee absenteeism due to TRP-related illness and increased employee productivity, and the anticipated costs to the health-care system saved due to less TRP-related illness, including mental health distress related to nicotine addiction. Different TRP have different health effects, chronic use of smoked tobacco being the leading cause of TRP-related morbidity and mortality and the highest priority in tobacco control. Hence, modelling should differentiate the impacts of prevention of initiation and cessation of use among chronic users for a variety of TRP. This could provide evidence about whether a youth-focused TRP regulatory policy merits prioritization if it both prevents uptake and chronic use of smoked tobacco products and has favourable impacts on cessation of smoked tobacco among adult chronic tobacco users. Additionally, some policies are misunderstood by the public due to uncertainty or to industry public relation campaigns. The misunderstanding can include concern that consumers will be subject to enforcement or penalties for purchasing banned TRP, while standard policy addresses enforcement for manufacturers, marketers, distributors and retailers *(180)*. It is important to remember, however, that all TRP pose risks to health, including the risk of addiction. Inclusion of youth voices to advocate for policy changes can be highly effective *(110,111)*.

2.5.2.2 Designing and implementing policies that are comprehensive, straightforward and adaptable to avoid loopholes and the burden on regulators

Any regulation on products based on flavouring or other characteristics and design or marketing restrictions can be made more effective, unambiguous and more difficult to evade if it specifies a limited set of industry practices and product specifications that are considered within legal limits. In this approach, any industry action or manufactured product that falls outside the legal limits would, by default, be banned. Such a strategy might be preferable to regulatory approaches that permit all practices or product specifications by default and ban specific practices

and products. The strategy of singling out banned practices and products is problematic because manufacturers, marketers and retailers can identify substitute practices that are not prohibited but have the same adverse impact on CYA as prohibited practices. Such a policy would have prevented TRP manufacturers from substituting synthetic coolants for menthol additives. A list of ingredients that are allowed in the manufacture of certain TRP, such as in Canadian TRP regulations, avoids concern about the development of novel compounds or practices that are yet to be identified.

Requirements for warning labels, listing of relevant ingredients and constituents, and the presence or potency of nicotine should be clearly specified in policies. Requirements for the size, text, font, location and other features of labelling prevent deviations that render such regulations less effective (e.g. text size too small to read easily). When possible, labels should be placed directly on the product and not only on the packaging, as CYA often obtain products removed from packaging by peers or third-party resellers. When possible, labels should be placed on each cigarette, heat stick, pouch sachet or e-cigarette device.

2.5.2.3 Prioritizing regulatory activities that target populations and products according to the principles of "anticipated impact and equity"

Although regulators may wish to set policies that cover all populations and products in their jurisdiction, they may have limited resources. In such circumstances, regulators can intentionally prioritize measures that provide the largest gains and the least inequity by applying the principles of "anticipated impact and equity".

In the Impact Principle, products with the highest combined prevalence of use and harm have the most adverse impact on population health. They are therefore of the highest regulatory priority. While much remains unknown about the relative harm of newer TRP, the harms associated with smoked TRP are well known and documented. When the prevalence of smoked and non-smoked TRP is similar, smoked TRP are often of higher priority for investment of resources. In countries that have not yet adopted CYA-focused regulatory policies on cigarettes although they smoke them, cigarettes should remain the priority product, as they are the most commonly used TRP. In countries with well-developed CYA-focused cigarette regulatory protection but no strong e-cigarette policy or in which there is concern about increases in both use and marketing of e-cigarettes, e-cigarettes might merit high priority.

The equity principle calls for prioritizing the CYA subpopulations that are most at risk of TRP uptake and of their health consequences due to industry targeting and other social determinants of health. Populations that disproportionately face discrimination or socioeconomic deprivation, such as Indigenous and low-income communities, and groups with other risk factors would benefit from additional consideration and resources when designing,

implementing and enforcing policies. Without prioritization, these groups might be overlooked, perpetuating TRP-related health inequity.

To identify products and population priorities consistent with the "impact and equity" principles, regulators can use surveillance data from their region on the prevalence of use of each TRP in the overall population and in specific subpopulations. Regulators can also leverage industry marketing surveillance data to identify CYA populations that are disproportionately targeted in marketing. Use of such data and other relevant sources can help regulators to develop a strategic plan for identifying priorities for allocating resources.

2.6 Discussion and conclusions

Several key points in this review of TRP use, prevalence, determinants and regulatory protections for the CYA population are discussed below.

First, the prevalence of CYA TRP use and of CYA-focused regulatory policies, mechanisms and enforcement varies widely among countries and products. Between 1999 and 2021, in countries that participated in several Global Youth Tobacco surveys, the prevalence of smoked tobacco use by both male and female youth decreased in more than half of the countries but increased or remained stable in about one fourth, which were predominantly lower-middle-income countries *(181)*. Use by youth of nicotine products, such as e-cigarettes, has recently increased in many countries, including in countries with no regulatory measures, as well as those in which cigarette smoking by CYA fell. Numerous countries do not conduct systematic surveillance of CYA use or assess use of only a subsection of TRP, limiting estimates of CYA TRP use. Although countries have rapidly increased enactment of youth-focused regulations of cigarettes and other smoked tobacco products, regulation of newer and emerging tobacco, nicotine and related products, such as e-cigarettes, nicotine pouches and HTP, has been slow and heterogeneous.

Secondly, although there is substantial global variation in the prevalence of and policies for use of TRP by CYA, the determinants of the appeal and abuse liability of TRP for CYA are generally universal. TRP with palatable flavours, sensory-modifying additives, higher nicotine delivery and youth-friendly designs appeal to CYA in many countries. Additionally, youth-oriented marketing, such as use of candy and other sweet flavours, youthful models and messaging about reduced harm and tobacco use as an aspirational, socially normative lifestyle are associated with CYA TRP use in various countries.

Thirdly, the comprehensiveness of each policy varies widely, as does the extent to which they are implemented and enforced, which may contribute to their impact. Countries with comprehensive bans on the sale of any product in a TRP class have a low prevalence of CYA use *(31,182,183)*. No clear estimates are available of the impact of policies on CYA use of TRP in countries with less

comprehensive restrictions on emerging products, except for flavour bans and taxation *(55)*. For example, bans on use of TRP in public places ("smoke-free") differ in whether they cover various TRP or only smoked tobacco and the extent to which they apply to public establishments. Furthermore, enforcement varies. It is plausible that differences in the breadth of policies and their enforcement determine their impact on use of TRP by CYA.

Fourthly, the products and practices of TRP manufacturers, marketers and distributors often evolve more quickly than regulations. Even well-intended policies may have loopholes or are insufficiently comprehensive, increasing the risk that manufacturers will quickly adapt their products and marketing strategies to comply with them; however, this undermines their effectiveness, such that synthetic coolant additives were substituted for menthol in TRP to remain compliant with bans. An emerging concern is the marketing of e-cigarettes, nicotine pouches and other TRP in which nicotine analogues are substituted for nicotine, so that the products are outside standard regulatory protection in some countries, even though the products potentially have similar determinants and health consequences to those of nicotine-containing TRP. Regulatory policies that are comprehensive and unambiguous and apply the same standards to all products may be less vulnerable to changes in TRP manufacture and marketing. Use of modern surveillance systems in which surveys are combined with tracking of TRP industry activities by monitoring social media, observing retailers and talking directly to youth about the TRP they observe being used by CYA in their communities can lead to policy modifications to protect CYA and prevent emerging trends from developing into population-wide epidemics.

Fifthly, interference by tobacco and related industries, including tobacco-funded organizations, such as intense lobbying, is a significant barrier to implementation of comprehensive policies. For example, finalization into law of the US FDA ban on menthol cigarettes and other characterizing flavours in cigars was delayed by political considerations since 2023 and has now been withdrawn *(184)*.

2.7 Research gaps, priorities for regulation and surveillance needs

2.7.1 Research gaps

While further research will strengthen evidence-based policy-making and help to protect CYA from the dangers of TRP, the need for additional studies should not delay or hinder timely implementation of regulatory measures. Instead, research and surveillance should proceed in parallel with policy action: ongoing surveillance to accompany, reinforce and prioritize regulations and research after their adoption to monitor their impact in order to make adjustments. Such research must be conducted with rigor and care to avoid misinterpretation due to confounding factors. Recommendations for future research include:

- quasi-experimental studies of the association between exposure and regulatory policies for CYA TRP use that include confounders and the possible synergy of several regulatory policies (on, e.g. flavour bans and nicotine concentration);
- studies of factors to strengthen the effectiveness of youth-focused policies on reducing the prevalence of use of TRP by CYA, such as enforcement and the breadth and specificity of policy and regulatory mechanisms;
- simulation studies to anticipate the reduction in prevalence of use or in the number of cases prevented by implementing specific CYA-focused policies; and
- studies of the collateral benefits or unanticipated consequences of youth-focused TRP policies on cessation of TRP use by CYA and older adults.

2.7.2 Priorities for youth-focused tobacco control and regulation

2.7.2.1 Develop and implement a comprehensive approach to reducing all aspects of TRP use by CYA

Cigarettes and smoked tobacco are a highly preventable cause of mortality and morbidity globally, often occurring disproportionately in lower-income countries and communities. To reduce use of cigarettes and other smoked tobacco products, policies for reducing youth smoking that are known to be effective should be adopted globally, with new, comprehensive, innovative policies. The rapid increase in marketing and CYA use of products such as e-cigarettes and smokeless TRP complicate CYA-focused tobacco regulation. Use of e-cigarettes by CYA has increased in several countries in which e-cigarettes were aggressively marketed in environments with limited regulatory protection. CYA use of nicotine pouches and other nicotine products has not reached prevalence levels commensurate with those of e-cigarettes but could rise in some countries with increased marketing and limited regulation. Widespread implementation of the regulatory approaches reviewed above and recommended by the WHO FCTC could reverse trends in CYA use of all TRP, including new products such as e-cigarettes and nicotine pouches. The findings of the proposed research will inform outcomes.

2.7.2.2 Reduce global health disparities associated with smoked tobacco use or smokeless tobacco by CYA without future increase in CYA use of other more recent TRP

International differences in tobacco-related disease are attributable, in part, to the persistently large numbers of CYA who initiate tobacco smoking in certain countries, especially those with disproportionately fewer financial resources. Similar disparities are noted in use of smokeless tobacco products, which is disproportionately high in some South-East Asian countries. Widespread implementation of the WHO FCTC-recommended policies to regulate smoked

and smokeless tobacco could prevent future generations of CYA from taking up these products in countries with disparities in tobacco-related health. It should be noted that countries that successfully reduced the prevalence of youth tobacco smoking later saw increases in the marketing and CYA use of e-cigarettes and other emerging TRP. Thus, countries that apply youth-focused regulatory policies to address smoked tobacco use should consider extending the policies broadly to various TRP to prevent future increases in CYA use of other products, while monitoring that this does not reverse the decline in cigarette use.

2.7.2.3 Implement and increase the effectiveness of youth-focused TRP regulatory policies

Understanding of the barriers that prevent adoption of WHO FCTC-recommended policies to protect CYA could help to improve technical support to overcome such barriers. Identification of best practices in ensuring retailer compliance and enforcement of youth-focused TRP regulations once introduced and education of retailers could augment the effectiveness of such policies. Identifying, addressing and preventing potential loopholes is essential to ensure the effectiveness of policies.

2.7.3 Surveillance needs and recommendations

2.7.3.1 Identify factors that contribute to high prevalence of use of TRP by CYA.

The recommendations include:

- surveillance of industry marketing practices to promote use of TRP by youth; and
- assessment of patterns of adoption and implementation of youth-focused regulatory policies to prevent use of TRP among youth.

2.7.3.2 Increase surveillance of emerging TRP classes, including HTPs, nicotine pouches, other nicotine products (e.g. nonmedicinal flavoured commercial nicotine gums and mints), and nicotine analogue products

The recommendations include:

- increased surveillance of prevalence of CYA use of emerging TRP globally;
- assessment of adverse health impacts associated with CYA use of emerging TRP; and
- increased identification and surveillance of changes in industry marketing approaches and in design and constituents.

2.8 Policy recommendations

2.8.1 To prevent use of and addiction to TRP by CYA, the following regulatory actions aligned with the WHO FCTC are recommended.

Countries that ban the sale of a TRP should strengthen implementation of the ban, continue monitoring and surveillance for public health interventions, and ensure strong enforcement.

Countries that permit commercialization of TRP as consumer products should ensure strong regulations, including:

- a ban on the manufacture (where relevant), import, distribution and sale of all TRP with characteristics that increase appeal, toxicity and abuse liability targeted at CYA, including:
  - non-tobacco flavours (e.g. candy, fruit, coolants, "concept" flavours), including menthol and analogues;
  - limiting the concentration and quantity of nicotine to reduce the risk of dependence;
  - additives or modifications that facilitate nicotine uptake, absorption or inhalation;
  - additives with carcinogenic, mutagenic or reprotoxic properties;
  - attractive and/or promotional features on the presentation and packaging of products, such as colours or colouring properties and attractive descriptors, including names;
  - filters;
  - TRP modified to have a pH < 8;
  - designs that enable discreet possession and use;
  - features that enable the user to manipulate the product after purchase;
  - designs that mimic items popular with CYA, such as toys, video games and school supplies; and
  - misleading or deceptive or unauthorized claims, such as on safety or efficacy for quitting cigarette smoking;
- a comprehensive ban on promotion and advertising of all TRP, as per Article 13 of the WHO FCTC, to close loopholes that enable use of new channels and venues:
  - no advertising, marketing or promotion via any non-digital or digital channel;
  - no public relation campaigns;
  - no advocacy or direct or indirect lobbying by the TRP industry to

governments; and
  - no public display of TRP in any retail outlet that can be entered legally by children;

- implementation of youth-focused policies that prohibit access, including:
  - laws on a minimum age for purchase ≥ 21 years;
  - sale of single rod or stick cigarettes, cigarillos, little cigars, HTP, *bidis* or other TRP;
  - sale of disposable e-cigarettes;
  - Internet sales;
  - vending machine sales;
  - requirement for sales to be from retail outlets in which consumers are required to be aged ≥ 21 years to enter;
  - a uniform taxation rate on all TRP;
  - no sales within 1 km of schools, child-care centres, hospitals and other areas frequented by children; and
  - a requirement for retailers to obtain a license to sell TRP;

- labelling requirements, including
  - clearly legible, large, visible, legislated research-based graphic health warning labels that cover a minimum of 50% of the packaging and the product and are fully coloured, rotated and in the principal national language;
  - labels that state the relevant ingredients and emissions, as defined by national authorities; and
  - labels and packaging that do not include quantitative or qualitative statements about tobacco constituents and emissions that might imply that one brand is less harmful than another; and

- a ban on use of all TRP in all public indoor and outdoor settings, in private vehicles in which there are children and in public places commonly frequented by children, including playgrounds, parks and beaches.

2.8.2 Considerations in adopting and implementing CYA-focused regulatory policies to improve their impact

Important considerations before and after implementation include emphasis on information campaigns to educate and remove public misconceptions and regular enforcement of regulations and monitoring of compliance. Equally importantly, users of TRP should be supported in quitting with approved cessation tools of proven efficacy and safety, including advice from health-care workers, toll-free

quit lines, mobile and digital cessation services and approved therapies. However, any policy mandating the use of such therapies must be carefully designed to avoid major health disparities related to cost and access.

A rigorous surveillance system should be maintained or strengthened to monitor changes in the market and in consumer behaviour and also to monitor industry interference to undermine regulations. This will not only strengthen countries' responses but will provide the necessary information to counter industry claims and arguments.

Comprehensive, forward-looking regulatory action is necessary to counter industry tactics and to protect public health, especially that of the most vulnerable segments, such as CYA. To prevent manufacturers from adapting their products to meet regulatory requirements but maintain their appeal to and addictiveness of CYA, policy-makers might consider a framework that provides a limited list of manufacturing practices and standardized product design specifications that are within regulatory bounds and ensure that any practice or product that is not on the list is banned. A list of standardized product characteristics rather than an exhaustive list of banned characteristics will discourage development of new flavouring chemicals, additives, modifications, designs and other practices to substitute for banned characteristics.

While there is sufficient evidence of the harm of new and emerging TRP to warrant immediate action, operationalization of certain policy guidelines may be incompletely understood. Given the lack of current research on these questions, countries that have prohibited import or sale could consider banning all products in these TRP classes as a precautionary measure until more evidence becomes available on the characteristics that limit appeal to and abuse liability by CYA. For countries that do not ban the sale of TRP, strict regulation of the products is recommended. Consistent regulations should be applied to all TRP.

As recommended in WHO FCTC Article 13, a widescale ban on promotion and advertising of all TRP is a robust means for preventing CYA from using them. To operationalize this policy, regulators might consider an explicit statement on where the products are to be placed in a retail outlet to avoid unintended promotion. This could include storing TRP without displays. Banning specific forms of promotion and advertising without comprehensive measures increases the possibility that manufacturers will identify new media that are outside the restrictions, such as web and social media marketing in environments where advertising restrictions were originally for television and other traditional media. It may be difficult to identify covert promotion on social media, such as influencers paid to promote TRP by companies, who may not publicly disclose their relations with industry. To address this aspect, government regulatory bodies could work with social media companies to identify solutions, such as restrictions on all pro-tobacco and pro-nicotine content and automated warning messages on any social media post that depicts any TRP to notify all viewers that the post depicts a TRP

and provide information about the associated risks.

Identification of all settings in which CYA might encounter TRP and their marketing might be difficult. Regulators could consider limiting sales to "brick-and-mortar" retailers who require a minimum age to enter the establishment (e.g. those that sell only tobacco and nicotine products). Regulators could also consider setting a maximum taxation rate on all TRP, in view of their health impact and their potential appeal to youth.

As CYA sometimes obtain unpackaged TRP, regulators might consider requiring that warning labels and other required labelling information be visible directly on the products (when possible) rather than only on the packages. For example, a label would be required directly on cigarette paper, heat sticks, e-cigarettes and HTP devices, nicotine pouch sachets and on oral nicotine products such as commercial nicotine mints, which could read "contains nicotine". Warning messages must be in language that is understood by young audiences. When possible, they should include messages on the adverse health outcomes that are relevant to CYA (e.g. addiction, mental health symptoms), graphic images, information on the concentration or amount of nicotine or other psychoactive chemicals and all ingredients, especially those considered hazardous or potentially hazardous.

Regulators might consider extending public use bans to all TRP except medicinal products, as CYA who encounter TRP use may perceive it as culturally and socially acceptable. As it is difficult to identify every public setting in which TRP use could be seen by CYA, regulators might consider banning TRP use in any setting other than residences.

To ensure that all the latest TRP and marketing activities are subject to regulation, policy-makers should consider comprehensive monitoring of TRP industry manufacture, marketing, sales and other activities as well as surveillance of CYA patterns of use of individual TRP.

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3. Flavours in tobacco and nicotine products: new developments, implications and regulation

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Contents

Abstract
3.1 Background
3.2 Methods
3.3 Epidemiology of flavoured products: frequency, patterns and reasons for use by sociodemographic variables
3.3.1 Updates on electronic nicotine and non-nicotine delivery systems
3.3.2 Updates on conventional smoked and smokeless tobacco products
3.3.3 Nicotine pouches
3.3.4 Heated tobacco products
3.4 Characteristics, properties and health effects of common flavours and implications for public health
3.4.1 Global definitions of flavours
3.4.2 Emergence of flavours without a traditional "taste" (e.g. synthetic coolants)
3.4.2.1 Chemical and physical properties of emerging synthetic flavouring agents
3.4.2.2 Toxicity of emerging synthetic flavouring agents
3.5 Marketing of flavours in tobacco and nicotine products
3.5.1 Conventional marketing of flavoured tobacco products
3.5.2 Newer marketing strategies for flavoured tobacco and nicotine products
3.6 Effects of flavours on appeal, abuse liability, experimentation, uptake and sustained use
3.6.1 Appeal
3.6.1.1 How flavour appeal supports experimentation and uptake
3.6.1.2 How flavour appeal differs for youth, young adults and adults who use tobacco (and who may be attempting to quit)
3.6.2 Abuse liability
3.6.2.1 Abuse liability and sustained use
3.6.2.2 Consideration of abuse liability in specific populations
3.6.2.3 Abuse liability of emerging flavoured products
3.6.2.4 How the form of nicotine impacts the appeal and abuse liability of flavours
3.7 Regulation of flavoured products
3.7.1 Case study:Netherlands (Kingdom of the)
3.7.2 Impact of regulation of specific flavoured products
3.8 Discussion
3.9 Research gaps, priorities and questions
3.10 Recommendations
References

Abstract

Tobacco and nicotine products contain flavour additives that can be used to enhance product appeal and can influence use. Flavours are highly prevalent in most smoked tobacco products (cigarettes, cigars, hookah) and electronic nicotine delivery systems (ENDS), and also in emerging products such as nicotine pouches and HTP. Flavours may increase the appeal of tobacco and nicotine products and their abuse liability, and marketing tactics may be used to enhance the appeal of flavours even before product initiation. Additionally, new and emerging additives, such as synthetic coolants, may alter the sensory experience of tobacco and nicotine products and also potentially subvert flavour regulations. Flavours in tobacco and nicotine products are regulated in various ways globally. This report on flavours in tobacco and nicotine products provides an update on the global prevalence of flavour use by product, new and emerging flavour additives and how flavours influence marketing, appeal and abuse liability. The report also addresses the structure and impact of current global flavour regulations.

Keywords: Nicotine, tobacco, flavour, additives, cigarettes, ENDS, cigars, nicotine pouch, heated tobacco products, menthol

3.1 Background

Most tobacco and nicotine products, including smoked and other products, contain added flavour chemicals that can change the product taste, ease harshness and improve the user's sensory experience of the product. Flavours and other sensory additives may enhance both the appeal and the abuse liability of tobacco and nicotine products and may do so differently according to age, race, sex/gender and history of tobacco product use. Flavour chemicals and additives may be toxic (depending on the concentrations used), which may contribute to the overall toxicity of tobacco and nicotine products. In our chapters in the seventh and eighth reports of TobReg *(1,2)*, we reported the prevalence of use, the sensory effects and global regulations on flavoured tobacco products. This chapter updates the information on use of flavours in tobacco and nicotine products, including the emergence of new synthetic coolant "flavours" and new flavoured tobacco and nicotine products, and on global flavour regulations. We also discuss how flavours and their marketing influence the appeal and abuse liability of tobacco and nicotine products. This report is not a systematic review but a descriptive overview of emerging issues in the use of flavours in tobacco and nicotine products. Furthermore, the focus is on added flavours and additives rather than on the flavours produced by tobacco itself.

As described in our chapter in the seventh report *(1)*, there is limited systematic global evidence on the availability and use of flavours in tobacco and nicotine products. That said, there are some known country and region-specific

differences in which flavouring chemicals are used. For example, conventional cigarettes may contain added cloves and oils in Indonesia (*kretek*); smokeless tobacco may contain added spices, oils, flavouring, betel nut and other ingredients in India (*pan masala*, *gutka*); and hookahs in the Middle East (but now also popular in Europe and North America) contain high levels of added sweeteners and flavours. Countries and regions also differ in how they define flavours, which, as discussed below, can create challenges for crafting and implementing regulations.

Globally, the definition of what constitutes an added flavour and whether a constituent is a flavouring agent differ. For example, the European Union (EU) defines the term "characterizing flavour" as a clearly noticeable smell or taste other than one of tobacco, resulting from an additive or combination of additives, including, but not limited to, fruit, spice, herb, alcohol, candy, menthol or vanilla, which is noticeable before or during the consumption of the tobacco product.

As discussed below, this definition may complicate categorization of new constituents that do not have detectable smell or taste but can still alter the sensory effects of tobacco or nicotine. Furthermore, the definition does not include consideration of low levels of flavour additives that do not have a distinctive taste or smell but may still alter the sensory effects of tobacco or nicotine *(3,4)*. Other countries, such as Brazil and Canada (*5,6)*, ban use of any additives identified as flavouring agents by the joint Food and Agricultural Organization of the United Nations (FAO)/WHO Committee on Flavour Additives or as "generally recognized as safe" flavouring agents by the Food and Extracts Manufacturers Association (FEMA) in the USA. The USA also prohibits use of additives (aside from menthol) that produce characterizing flavours in cigarettes or their components and has considered (but not approved) a comprehensive definition of flavours in cigars that includes all artificial and natural flavour additives that produce multisensory user experiences and representations of flavours in labelling and advertising *(7)*.

Countries also differ in terms of whether some flavours, such as menthol, are excluded from restrictions on tobacco and nicotine product flavours and on which tobacco and nicotine products are covered by flavour regulations. ENDS and nicotine pouches may be regulated differently from products that contain tobacco. For example, Brazil and Canada have banned all flavouring chemicals, including menthol, in all tobacco and nicotine products, including ENDS and nicotine pouches (with the exception of traditional alcohol flavours in Canada) *(5,6)*. In the EU and in the Republic of Moldova and Türkiye *(8,9)*, the restriction on flavours does not extend to other tobacco products such as cigars, cigarillos, little cigars and smokeless tobacco products. Since 2023, however, the EU has included HTPs in its provisions to restrict flavours *(10)*. In the USA, federal regulations ban all flavours except menthol in cigarettes and roll-your-own tobacco, and some state and local regulations (e.g. in Massachusetts and in San Francisco, California) ban all flavours, including menthol *(7,11)*, in all tobacco products.

3.2 Methods

For the current report, we reviewed the literature on flavours in tobacco and nicotine products published since the previous TobReg reports *(1,2)* between January 2021 and October 2024. Several search engines were used, including PubMed, Google Scholar and Web of Science. As this is a narrative review of the current literature rather than a systematic review, publications on the current landscape of flavoured tobacco were selected. When there were no global data (e.g. studies that represented outcomes only in the USA), this is noted. Relevant information on the regulatory status in Member States was updated during the review with the most recent data from the WHO report on the global tobacco epidemic, 2025 *(3)*.

3.3 Epidemiology of flavoured products: frequency, patterns and reasons for use by sociodemographic variables

While flavoured tobacco and nicotine products are widely used globally, systematic reporting of prevalence rates by countries remains limited. Much of the available data are from the USA and indicate that flavoured tobacco product use is common among both youth and adults, although it can present itself differently in various sub-populations *(12)*. Among adults, data from the 2019 Tobacco Use Supplement to the Current Population Survey (TUS-CPS) indicate that 79.0% of ENDS users (4.1 million), 56.3% of pipe users (0.61 million), 51.7% of smokeless tobacco users (1.7 million) and 26.9% of cigar users (0.97 million) reported use of a non-tobacco flavour within the past month, and one third (33.8%) of current cigarette users smoke menthol-flavoured cigarettes *(13)*. Among youth, the rates of flavour use are even higher. In the US National Youth Tobacco Survey 2024, use of ENDS and nicotine pouches with non-tobacco flavours in the past month was 87.6% and 85.6% respectively *(14)*. Comprehensive evidence on flavoured tobacco and nicotine product use worldwide is essential.

3.3.1 Updates on electronic nicotine and non-nicotine delivery systems

Nearly all ENDS contain some form of added flavouring agents to create flavours, including sweet, cooling and tobacco (unlike in other tobacco products, additives are used to produce a "tobacco" flavour in ENDS). ENDS are available in single- or multi-flavour combinations. In the International Tobacco Control (ITC) surveys of smoking and vaping, fruit flavour was very popular in ENDS in Canada, Malaysia and the USA. Notably, although the size of the populations differed slightly, the prevalence of use of fruit-flavoured ENDS use was 39.0% in Canadians aged ≥ 15, 88.8% in adults aged ≥ 18 in Malaysia and 36.4% in the US population aged ≥ 18 *(15–17)*. Use of menthol- or mint-flavoured ENDS was also common, with minimal differences in the rate of use among adults in Australia, Canada, England and the USA (29–44%) and a rate of 54.9% observed in Malaysia *(16,17)*.

Youth and young adults appear to use flavoured ENDS at higher rates than adults *(13,18)*. Data from multiple waves of the Population Assessment of Tobacco and Health (PATH) study in the USA showed that the rates of use of fruit-flavoured ENDS were highest among youth (12–17 years, 67.8–71.9%), followed by young adults (18–24 years, 56.2–64.4%) and adults aged ≥ 25 years (34.7–46.3%) *(18)*. A similar pattern of decreasing use by age was seen among adults, TUS-CPS data showing a graded decrease by adult age group (18–24, 25–34, 35–44 and ≥ 45) in non-tobacco flavoured ENDS *(19)*. The PATH study also showed higher rates of initiation of ENDS use with non-tobacco flavours among younger populations, including adolescents (71.9%) and young adults (57.6%), than in older adults (44.6%) *(20)*. Sex-related differences in flavoured ENDS use have also been observed. In a recent review of global data, it was found that females favour fruit and menthol flavours over tobacco, while males are more likely to prefer tobacco flavours *(21)*. While not all studies found sex differences in ENDS flavour preferences *(22)*, the pattern underscores the need for further research into sex differences in flavour preferences and tobacco product use. Differences in flavoured ENDS use may also be associated with smoking status (current, former or never smoker), never smokers initiating with sweet or fruit flavours and former smokers gravitating towards menthol or tobacco-flavoured ENDS *(23,24)*. The role of flavoured ENDS in smoking cessation is, however, unclear. A recent global review showed a low level of certainty that flavoured as compared with non-flavoured or tobacco-flavoured ENDS increased the likelihood of quitting intentions or attempts *(24)*.

Multi-flavour ENDS, in particular "ice"-flavoured products, have gained significant popularity in recent years *(25–30)*. "Ice" products combine a sweet flavour with cooling or minty flavouring chemicals, creating a distinctive sensory experience that appeals to a wide range of users. Although global data on the prevalence of multi- and specifically "ice" flavour use are limited, these products are growing in popularity in the USA. Evidence from the 2023 National Youth Tobacco Survey showed that, of students aged 13–18 years who currently used ENDS, over half preferred "ice" flavours *(30)*. Similarly, a study in Los Angeles (CA), showed that, among current young adult ENDS users (mean age, 21.2 years), 48.8% primarily used "ice" flavours *(25)*. These findings indicate the growing appeal of multi-component flavours, particularly among younger populations. Additionally, recent evidence suggests differences in flavour preferences by age group, younger users preferring "ice"-flavoured ENDS and older users showing a stronger preference for menthol or tobacco-flavoured ENDS *(25)*. In the USA, use of "ice" flavours by youth and young adults has been associated with an increased frequency of ENDS use, greater nicotine dependence and higher odds of dual use with conventional cigarettes, as compared with users of non-"ice" fruit or sweet flavours *(30)*. These findings suggest that "ice" flavours contribute to sustained ENDS use.

Limited information is available on the prevalence of use of electronic non-nicotine delivery systems (ENNDS) or on the use of flavours in these products, as few countries have reported such data. Rates of ENNDS use are very low, daily use being < 2% in Canada, the United Kingdom and the USA *(31)*. Recent evidence from the USA indicated that, among ENNDS users, the most commonly used flavours were sweet, dessert or candy flavours (ever use, 36.3%) and fruit flavours (ever use, 33.4%) *(32)*. Although ENNDS are not further mentioned in this paper, most of the considerations on flavoured ENDS are equally applicable, as ENNDS are largely indistinguishable in design and are almost exclusively flavoured.

3.3.2 Updates on conventional smoked and smokeless tobacco products

Flavours are generally less varied in conventional tobacco products than in ENDS. In conventional tobacco products, the tobacco itself has a specific flavour, which is not considered a flavour additive. In the 2018–2019 TUS-CPS, 56.3% of adults who used hookahs used flavoured products, as did 51.7% of smokeless tobacco users and 26.9% of those who used cigar products. Younger adults were disproportionately represented among users of non-tobacco-flavoured products, particularly cigars and smokeless tobacco, rather than those who used tobacco-flavoured products *(13)*. Furthermore, in the USA, initiation of use of non-tobacco-flavoured cigars and smokeless tobacco was notably higher among youth than among adults aged ≥ 25 years *(20)*. Other studies in the USA have also shown that menthol-flavoured cigarette use is significantly higher in certain demographic groups, including adults who are black, of Hispanic ethnicity or female and those who are lesbian/gay, or have serious psychological distress, and in youth and younger adults *(14,33)*. Data from a survey by International Tobacco Control (ITC) in eight European countries also showed a graded decrease in menthol cigarette use among adults by age, with 11.9% of 18–24-year olds who smoke using menthol cigarettes, which decreased to 9.6%, 5.5% and 5.1% among those aged 25–39, 40–54 and ≥ 55 years, respectively *(34)*. Evidence suggests that implementation of menthol bans can lead to a decrease in the use of flavoured conventional products, particularly cigarettes *(35,36)*. Evidence from Great Britain, which banned menthol cigarettes in 2020, suggests, however, that in 2023 (as compared with 2020) there was a non-significant decrease (16% to 14%) in menthol cigarette use among adults who smoke, with a greater decrease among younger adults aged 18–24 years (from 26% to 19%) *(37)*. Data from areas with less stringent regulations indicate that flavoured conventional tobacco products remain very popular among younger people *(38)*. These findings underscore the role of flavours and flavour regulations in sustaining tobacco use.

Flavour accessories, such as capsules and cards, are often used to enhance the flavour of tobacco products such as cigarettes *(39,40)*. Flavour capsules are small crushable beads that are embedded in cigarette filters and release bursts of

flavour when activated, offering consumers a customized smoking experience. A systematic review showed that use of flavour capsules is most prevalent in Chile and Mexico, where approximately 40% of smokers reported their use *(39)*. Menthol is the most common capsule flavour *(41)*; however, other options, including some with vague "concept" descriptors, such as "Fusion Blast", have flooded markets, particularly in low- and middle-income countries *(42)*. Studies in Guatemala and Mexico showed menthol concentrations in these capsules that were 33 times higher than the next most common flavour additive, limonene *(41)*. Similarly, flavour cards, which are inserted into cigarette packs to transfer flavours into the cigarettes, have gained popularity, even in regions with strict bans on flavoured cigarettes, such as Canada, which prohibited menthol cigarettes in 2017 *(40)*. Brands of flavour cards such as Itsa are increasingly being adopted globally. These products extend the availability of flavoured tobacco products, circumventing regulations to restrict flavours. To mitigate their impact, research should be conducted to evaluate the prevalence and health implications of these products, particularly in low- and middle-income countries where regulatory oversight may be limited.

3.3.3 Nicotine pouches

Nicotine pouches, a new type of nicotine product, have gained global attention due to their marketing, unique design and flavour options. These opaque pouches typically contain nicotine, flavourings and other ingredients. Their appeal is increased by the inclusion of a wide variety of flavours *(43)*, including sweet (e.g. citrus, berry), mint/menthol (e.g. peppermint, spearmint), spice (e.g. coffee, cinnamon) and other non-specific flavours such as Zyn's "Smooth" and "Chill" labelled pouches, which are added for the sensory experience rather than a specific taste *(44)*. Some brands offer multi-flavour options, such as Velo's Breezy Mango and Icy Berries in the United Kingdom *(43)*. While rates of nicotine pouch use are still low, emerging evidence already suggests a preference for flavoured options. For example, in the 2024 US National Youth Tobacco Survey, 1.8% of youth reported current use of nicotine pouches, but, of these, 85.6% preferred flavoured options, mint being the most popular, followed by fruit flavours *(45)*. Other evidence suggests that youth use of flavoured nicotine pouches may be higher in certain regions (e.g. in southern California, USA) and in certain subgroups (e.g. youth who use other tobacco products) *(46,47)*. Nicotine pouch use also rose in Great Britain between 2020 and 2021, with 1 in 400 adults reporting use of nicotine pouches in the past month and the rates being higher in younger age groups, men and people who used other tobacco products *(47)*. In 2024, the rates were found to be higher, with 1 in 100 adults using nicotine pouches *(48)*. Global trends in the prevalence of use of nicotine pouches and the role of flavours in nicotine pouch use are not well studied. The available data suggest that flavoured options are a key driver of their popularity, particularly among youth and young adults, mirroring trends in the use of flavoured e-cigarettes and other tobacco and nicotine products.

3.3.4 Heated tobacco products

Since publication of the previous TobReg reports, the availability of HTPs has become more restricted in several regions, such as the EU, which has banned flavours in HTPs, and the USA, where there is ongoing litigation *(10,49,50)*. The sale of HTPs is prohibited in 24 countries, including Australia, India and Singapore. Of those countries that allow the sale of HTPs, 29 restrict the use of flavours in the products *(3)*. HTP manufacturers often use concept-based, non-characterizing flavour names to market their products, such as Ploom's "purple", "azure" and "amber", Glo's "scarlet", "green" and "ruby" and IQOS's "amber", "blue menthol" and "green menthol". The synergy of appealing imagery, enticing names and flavouring chemicals enhances the attractiveness of HTPs to a broad audience. Data on flavour use and the overall prevalence of HTPs remain limited. Recent statistics from the USA show that 8.9% of adults have ever used HTPs, and 3.0% are current users *(51)*. The 2020 Eurobarometer survey, conducted in 28 European countries, found that 6.5% of participants had ever used an HTP, and 1.3% were current users *(52)*. Data from the 2018 ITC survey, which included respondents from Australia, Canada, the United Kingdom and the USA, show that 39.9% of users lived in England, 27.1% in Canada, 21.4% in the USA and 11.7% in Australia *(53)*. Demographic analyses show that current HTP users are more likely to be younger and male. Smoking history also influences adoption of HTP, as current and former smokers are more likely to use HTPs than never smokers *(52)*. Data from the 2018 ITC survey in Japan showed that adult HTP users who also smoked cigarettes preferred menthol-flavoured HTPs *(54)*, which may indicate a role for flavour as a bridge between tobacco products. Trends in HTP marketing, such as the transition to colour-coded labelling instead of explicit flavour names *(55)*, may complicate regulatory oversight of flavours. Such changes should be investigated further to determine their impact on user perceptions and behaviour and public health outcomes. Longitudinal studies are essential to monitor evolving trends and assess the implications of these marketing strategies globally.

3.4 Characteristics, properties and health effects of common flavours and implications for public health

3.4.1 Global definitions of flavours

As stated above, flavours in tobacco and nicotine products have often been defined as having a "characterizing" taste and aroma and have been categorized by flavour type with various tools, including flavour libraries for smoked tobacco products and flavour wheels for ENDS *(56–58)*. These tools are used to identify categories (e.g. menthol/mint, fruit, dessert) of flavours in tobacco products and associated flavour additives (e.g. limonene, vanillin). Tobacco and nicotine products may fall into several flavour categories and may also have several components (e.g. watermelon–ice in both fruit and menthol/mint flavour categories). Flavour

additives can have unique, individual health effects and toxicity, especially when they are inhaled, as we noted previously *(2)*. The FEMA, an association of the US flavour industry, has noted that, while flavour additives may be labelled as "generally recognized as safe", this designation is for human ingestion and not for exposure by inhalation *(59)*. Below, we address the emergence of new flavour additives with unique sensory effects that do not meet the traditional definition of a flavoured product with a taste or aroma.

3.4.2 Emergence of flavours without a traditional "taste" (e.g. synthetic coolants)

Addition of synthetic coolants as flavouring additives in tobacco and nicotine products has been increasing over the past few years. Unlike conventional cooling additives, synthetic coolants do not impart a characterizing taste or smell but impart a perception of cooling in the mouth and/or throat (27). Therefore, and importantly, they do not fit into many current definitions of flavours, which refer to taste or aroma.

Synthetic coolants were developed in the 1970s by Wilkinson-Sword (WS) to impart cooling in shaving products without a distinguishable odour (60,61). Although these additives were not commonly used in commercially available tobacco products until recently, tobacco industry documents suggest a longstanding interest in WS compounds (62).

WS additives include the compounds WS-23, WS-3 and WS-5. WS-23 and WS-3 have been detected in both disposable and refillable ENDS products. The products include those with labels that suggest that they contain cooling agents, indicated by descriptors or labelling such as "ice", "chill" and "freeze" (63), and those with no indication of cooling, with names such as "Pomegranate", "Sour Apple" and "Grape" (64). Interestingly, there appear to be global differences in the use of synthetic coolants. JUUL ENDS sold in the EU contain synthetic coolants, while those sold in Canada and the USA do not (65).

Synthetic coolants have also been identified in nicotine pouches and conventional cigarettes, notably in jurisdictions that have banned menthol or cooling "flavours". For example, in the USA, after the ban on flavours in tobacco products in the states of California and Massachusetts, WS-3 was detected in cigarettes that were advertised as mentholated cigarette substitutes (e.g. "Non-menthol Green") (66). WS-23 was also detected in conventional cigarettes in Germany (67,68). In the USA, synthetic coolants (i.e. WS-3) have been detected in nicotine pouches such as Zyn brand pouches with concept flavour names such as "Chill" and also in combination with menthol and other flavourants in other Zyn brand pouches, with names such as Spearmint, Peppermint, Cool Mint and Menthol. Notably, the "Chill" Zyn brand nicotine pouch product has been advertised as "flavour ban approved" (69).

Synthetic coolants have unique flavour profiles, as they do not impart a flavour in the traditional sense via the retronasal cavity but rather produce a chemosensory experience. While the popularity of coolants has risen in recent years, there is limited information on how alteration of the sensory experience affects product use. In initial laboratory examinations in the USA in which the synthetic coolant WS-23 was compared with menthol and non-menthol additives in ENDS products, WS-23 enhanced "liking", willingness to use and cooling and reduced irritation more than either menthol or non-menthol ENDS (70). Given the proliferation of synthetic coolants in commercial tobacco and nicotine products, further examination of their use and intersection with other common flavourings (e.g. fruit, menthol) is warranted. Further, additional surveillance should be conducted of all tobacco and nicotine products, especially in countries and jurisdictions in which flavour bans either exclude particular additives (e.g. menthol) or describe flavours in a way that may leave a loophole for these unique compounds.

3.4.2.1 Chemical and physical properties of emerging synthetic flavouring agents

Structurally, WS synthetic coolants are derivatives of menthol and are based on the *p*-methane structure, the basic monoterpene structure of menthol *(64)*. Like menthol, the cooling effects of these synthetic coolants appears to be produced by a pharmacological interaction at the transient receptor potential melastatin subtype 8 (TRPM-8) protein, which is a cold and menthol receptor in humans. TRPM-8 is expressed in sensory nerve endings in the oral cavity and upper airways, and activation of the receptor produces cooling, analgesic and anti-inflammatory effects. Synthetic coolants vary considerably in their effects at the TRPM-8 and their strength of cooling. Like menthol, but with less efficacy, some synthetic coolants also activate transient receptor potential ankyrin 1, the sensory irritant receptor. Most of the literature on synthetic coolants has addressed topical effects, and there is limited information on their functionality when administered orally or by inhalation. There is even less information on how differences in structure result in differences in user experiences when they are present in tobacco and nicotine products *(64)*.

3.4.2.2 Toxicity of emerging synthetic flavouring agents

Flavour additives in ENDS can increase the general toxicity of aerosols, as detailed in the previous report on this topic *(1)*. Less is known about the toxicity of synthetic coolants. While several of the commonly used synthetic coolants (e.g. WS-3, W-23, W-5) are generally recognized as safe by FEMA for use in edible or topical preparations, the designation does not extend to the safety by inhalation exposure, especially in combination with tobacco and nicotine *(59,63)*. A review of studies on synthetic coolants suggested that the levels of these coolants in ENDS

products are sufficiently high to exert possible toxicological effects; however, further research is necessary on the inhalation toxicity thresholds of synthetic coolants *(64)*.

Emerging synthetic coolants are thus unique, in that they are "odourless" and have no traditionally "detectable" taste or aroma and instead impart a specific chemosensory experience (i.e. cooling). The evidence suggests that definitions of flavours must be extended beyond additives that alter taste and aroma to include those that alter chemosensory experiences.

3.5 Marketing of flavours in tobacco and nicotine products

Strategies for marketing flavoured tobacco and nicotine products have evolved to reach a wider range of consumers. While traditional channels, such as point-of-sale advertising and print media, remain effective, digital platforms and advanced marketing techniques have extended the reach of flavoured products, allowing more personalized engagement and targeting of specific demographic groups. Below, we review both well-known and newer strategies used to market flavoured tobacco and nicotine products and examine strategies used to attract and retain customers in various demographic groups.

3.5.1 Conventional marketing of flavoured tobacco products

In the past, tobacco companies have used established marketing channels to promote their flavoured products, focusing on visibility, brand loyalty and strategic placements. Despite advances in digital advertising, these conventional methods remain a cornerstone of their marketing and sales strategies for flavoured tobacco and nicotine products.

Point-of-sale (POS) advertising is an important strategy for promoting tobacco and nicotine products *(71,72)*. The industry uses visually striking displays of branded items, strategic product placement and aggressive price promotions to attract consumers *(72)*. An analysis of POS marketing in 42 countries in the six WHO regions between 2015 and 2021 showed that in 76% of countries, such advertising prominently included flavoured cigarettes, especially in Europe and South America *(72)*. In the USA, nearly all hookah sales by retailers were of flavoured products *(73)*; flavoured hookah tobacco was often bundled into multi-pack deals or sold at lower prices than unflavoured variants. These marketing strategies often emphasize the sensory appeal of flavours, such as menthol's coolness or cherry's sweetness. POS marketing often targets youth and young adults through flavour-centred imagery and discounts to make the products more affordable *(72,74,75)*. In the USA, gas stations and convenience stores that prominently display menthol cigarettes, flavoured cigars and e-cigarettes in colourful packaging, with discounts and loyalty programmes have been observed to have the greatest market share of tobacco sales *(76)*. Flavoured products are

often strategically placed on countertops or near candy displays, so that they are visible and accessible, particularly to youth *(77)*.

Print advertisements in lifestyle magazines and on billboards have vibrant imagery and targeted messaging to promote flavoured tobacco and nicotine products. For instance, there is a long history of marketing menthol cigarettes and cigarillos to African–American communities in the USA in culturally relevant campaigns in print media and on billboards *(78)*. The ads frequently feature images that appeal to those communities, such as community gatherings, music events and prominent cultural figures, with themes of coolness, relaxation and high social status *(78–82)*. These tactics continue to be used to market menthol cigarettes *(82)*.

3.5.2 Newer marketing strategies for flavoured tobacco and nicotine products

With advances in digital technology and social media, tobacco and nicotine companies have adapted their marketing strategies to use these modern tools. Approaches such as digital platforms, e-commerce, content marketing and experiential marketing allow greater personalization and direct engagement and can also reach younger, digitally connected audiences.

Digital platforms such as Instagram, TikTok and YouTube have transformed how tobacco and nicotine products are marketed, so that brands can engage global audiences through targeted, interactive campaigns *(83–85)*. For example, influencers and celebrities on these platforms promote tobacco and nicotine products as part of their lifestyle, often without disclosing sponsorships or paid partnerships. In Indonesia, YouTube influencers known as "e-cigarette reviewers" create engaging content that combines humour, product reviews and lifestyle narratives to promote flavoured e-cigarettes *(84)* and make them appear trendy and socially acceptable. Influencers on Instagram and TikTok in Sweden promote unique flavours such as elderflower and mint in smokeless tobacco products *(86)*. Tobacco companies have used paid influencers to promote cigarettes and HTPs on platforms such as Facebook, Instagram and Twitter in over 40 countries, circumventing advertising restrictions and reaching younger, impressionable audiences *(87,88)*.

Tobacco and nicotine companies are using sophisticated data analytics to track users' online activity and send personalized, targeted ads according to factors such as geographical location, age and browsing habits *(89)*. Flavoured tobacco and nicotine brands are also advertised in bright colours to attract youth on platforms such as TikTok *(90)*. The campaigns emphasize the sensory appeal of fruity or minty flavours and position their products as fun and fashionable, especially in countries with weak advertising regulations, such as Indonesia, Philippines and countries in eastern Europe *(91,92)*. The low cost of digital ads and minimal regulatory oversight allow tobacco and nicotine companies to reach large young audiences relatively easily, making digital marketing a powerful tool. Platforms

such as Netflix and Disney have committed themselves to reducing portrayals of tobacco and nicotine in content aimed at younger audiences, reflecting growing concern about the normalization of use of tobacco and nicotine in media *(93,94)*. Challenges raised by digital marketing require stricter regulations on the marketing of these products to youth and strategies to mitigate their influence.

As e-commerce develops, tobacco and nicotine companies are increasingly using direct-to-consumer platforms to market and sell their products. Online shopping platforms not only offer convenience but enable companies to control branding, customer engagement and user experience. Online retail cannot ensure effective age-gating, and youth can therefore purchase tobacco and nicotine products without adequate age verification. Subscription services and personalized product bundles allow regular shipment of products, often with exclusive promotion of different flavours *(95,96)*. In South-East Asia, e-commerce is a growing sales channel *(75)*. A study of online e-cigarette sales in Malaysia, Philippines and Thailand in 2014 showed that e-commerce sites and user-driven platforms such as YouTube and Reddit are key channels for promoting e-cigarettes. The top-ranking online retailers and forums were based mainly in China for Hong Kong and global consumers, while those for Malaysia, Philippines and Thailand were located predominantly in the United Kingdom and the USA *(97)*. These platforms market devices and e-liquids with discounts, coupons, diverse flavour options and user testimonials. E-commerce provides access to extensive consumer data, so that companies can refine their marketing strategies with tailored deals, product suggestions and promotions designed to increase retention.

Tobacco and nicotine companies also use other cutting-edge marketing strategies, such as content marketing, gamification and experiential marketing, to promote tobacco and nicotine products in global markets. Content marketing leverages social media and digital platforms to craft lifestyle-driven narratives. For instance, most of the transnational tobacco companies market nicotine pouches with various flavours in the United Kingdom as trendy lifestyle products *(98)*. The campaigns often include sleek visuals and hashtags to build a youth-oriented brand identity. Experiential marketing immerses consumers in events that connect them directly to products. In the United Kingdom, the launch in 2019 of the "Nordic Spirit" nicotine pouch with flavours was accompanied by a comprehensive marketing campaign, including sponsorship of major music festivals and promotional events at which free samples were distributed *(99)*. By 2021, Nordic Spirit had become a major nicotine pouch brand in the United Kingdom by using these immersive marketing strategies. Similarly, in the USA, flavoured e-cigarettes and nicotine pouches are marketed at concerts and sporting events, blending product appeal with leisure and entertainment *(99)*.

Marketing of flavoured tobacco and nicotine products combines established, non-digital strategies with digital and experiential approaches to

engage diverse audiences. Flavour-related advertising should continue to be monitored, through both non-digital channels and newer digital platforms, to better understand industry tactics and customer exposure. Comprehensive bans on flavoured tobacco and nicotine product marketing may help to reduce youth engagement.

3.6 Effects of flavours on appeal, abuse liability, experimentation, uptake and sustained use

3.6.1 Appeal

Appeal, or how much a product is liked, impacts tobacco and nicotine product use, especially initiation. The addition of flavour additives has been shown to differentially enhance appeal as a function of age, population and tobacco and nicotine product type *(1)*. Furthermore, flavour additives are not equal and can affect appeal differentially.

3.6.1.1 How flavour appeal supports experimentation and uptake

As noted in our previous report *(2)*, the appeal of flavour contributes to both experimentation and uptake of tobacco and nicotine products. Nicotine, the addictive constituent of these products, is usually aversive to naive users as it can produce negative effects such as irritation of the mouth and throat *(100)*. Flavours not only have independent appeal but also mask the negative effects of nicotine and thus have additive appeal for use of nicotine. Furthermore, flavour imagery and product marketing can enhance their appeal even before use of tobacco and nicotine products (see section 4). Reviews on this topic suggest that flavours not only increase appeal but also reduce perceptions of harm *(101)*. A recent qualitative study indicated that flavours appeal to both users and non-users. Users reported that flavours not only have qualities described as refreshing, pleasant and sweet but also can mask the "traditional tobacco" smell. Non-users reported that tobacco and nicotine products with various flavours smelled good *(102)*. Exposure of youth with and without experience of tobacco to images of fruit- and sweet-flavoured ENDS products increased their appeal (i.e. how "liked", "fun", "interesting" and "tasty" the products were) and the susceptibility of the young people to future use *(103)*. This observation is in line with evidence that flavours, specifically candy, dessert, fruit and fruit-ice type flavours, increase youth's willingness to try ENDS *(104)*. Similar patterns of flavour appeal are observed with emerging tobacco and nicotine products, such as nicotine pouches. Among young adults and adult tobacco users, flavour labelling on nicotine pouches enhances their appeal and willingness to use *(105,106)*.

3.6.1.2 How flavour appeal differs for youth, young adults and adults who use tobacco (and who may be attempting to quit)

While flavours have been shown to encourage experimentation and uptake of smoked tobacco products, flavours in other products (e.g. ENDS, nicotine pouches, HTPs) may also increase their appeal and use by adults who smoke cigarettes and who want to quit or reduce their cigarette use. There is very limited evidence on whether flavours impact the transition from cigarette to ENDS use *(107–109)*, although some evidence suggests that flavours are not necessary for product shifting by adults who use smoked tobacco products *(110)*. A comparison of adults who smoked but did not use ENDS with those with ENDS experience showed differences in the appeal of flavours, tobacco flavour being rated as more appealing than all other flavours (e.g. strawberry, vanilla, peppermint), suggesting that, for adults who use smoked tobacco, non-tobacco flavours in ENDS may not be as relevant for appeal as among youth *(110)*. In a study of Dutch non-smoking youth and adults who smoked cigarettes, although both groups gave higher ratings of appeal for sweet and minty ENDS flavours than tobacco flavour, tobacco ENDS were rated as more tolerable by adults who smoked than by non-smoking youth *(111)*. The data collected were primarily from those who smoked non-menthol cigarettes. While more data are necessary to fully understand these findings, current evidence suggests that smokers of non-menthol tobacco products may not require non-tobacco flavours to switch to use of other tobacco and nicotine products.

3.6.2 Abuse liability

The relation between flavour, tobacco and nicotine product appeal is important in view of the link between appeal and experimentation and an initial positive response to tobacco and nicotine products. The impact of flavour on tobacco and nicotine product abuse liability is also important. Abuse liability goes beyond initial appeal and is related to how a product maintains repeated use and sustain patterns of self-administration. Methods of measurement or determination of abuse liability intersect with measurements of appeal; however, metrics and investigations of maintenance of product use, beyond "liking", are specific to abuse liability. Nicotine is the dependence-producing constituent of tobacco and nicotine products, which contributes to abuse liability and maintains product use. Less is known about how flavours contribute to the maintenance of use or how flavours and nicotine interact to alter abuse liability. The limited evidence suggests that flavours alter abuse liability differently as a function of nicotine concentration *(112)*.

3.6.2.1 Abuse liability and sustained use

The availability of data on the role of flavours in product abuse liability depends on the tobacco product. Most research has been conducted on the role of menthol in smoked tobacco products, as menthol is a common flavour in these products. In two recent studies *(113,114)*, behavioural economic measures of product demand were used to determine the abuse liability of menthol cigarettes, non-cigarette menthol products (e.g. little cigars) and non-menthol cigarettes among menthol cigarette smokers. In both studies, smoking of non-menthol cigarettes resulted in less product demand than smoking of menthol cigarettes, and demand for non-menthol cigarettes was sometimes lower than that for other menthol smoked tobacco products (e.g. little cigars). These findings suggest that menthol flavouring can increase the abuse liability of smoked tobacco products, particularly among current users of menthol cigarettes. Other research on people who smoke menthol cigarettes shows that, when the menthol content in cigarettes is restricted, people change to using other menthol-containing tobacco and nicotine products, including both smoked (e.g. little cigars) and non-smoked (e.g. ENDS) products *(115)*. This suggests that menthol products maintain behaviour more strongly than unflavoured products among people who prefer menthol cigarettes. In another comparison of use of sweet-flavoured and unflavoured cigarillos by young adults, the abuse liability was higher with flavoured cigarillos, resulting in increased use (i.e. more puffs taken) *(116)*.

Investigations of the abuse liability of ENDS show a similar pattern, that flavour may enhance abuse liability and support continued use. In a study in the USA of youth who had used JUUL (when JUUL was available in the USA in a variety of flavours), those who continued use reported liking JUUL flavours significantly more than those who had tried JUUL but had not persisted in use *(117)*. Flavour type has been shown to enhance abuse liability, although the results differ among studies. Surveys of high-school students and young adults have shown that cooling or mentholated products maintain ENDS use and that use of cooling products is associated with increased e-cigarette use and dependence *(118,119)*. Laboratory data, however, showed that sweet flavours result in more ENDS use than menthol *(120)*. More research may be required to understand differences among flavours.

3.6.2.2 Consideration of abuse liability in specific populations

The abuse liability of flavour may differ as a function of demographics. For example, flavour may be more important in the abuse liability of tobacco and nicotine products among female than among male users *(121–123)*. In an extended study of women who smoked menthol cigarettes who were assigned to menthol or non-menthol cigarettes with or without reduced nicotine levels, those assigned to menthol cigarettes with reduced or normal nicotine content had higher smoking

rates during the study than those assigned to non-menthol cigarettes with reduced or normal nicotine content. By the end of the study (6 weeks), however, those assigned to reduced nicotine content menthol cigarettes had decreased their smoking rates to levels congruent with non-menthol conditions *(124)*. This suggests that, for women, who generally have more difficulty in quitting tobacco use *(121)*, menthol may maintain tobacco use for at least some time, even if nicotine levels are reduced. A similar pattern was observed among women in an evaluation of ENDS products. The reward was greater for women who smoked (either menthol or non-menthol) after exposure to menthol flavoured e-cigarettes than after exposure to sweet- and tobacco-flavoured products. A similar difference was not observed for men. In the same study, no marked difference by sex was found in measures of appeal, suggesting that menthol specifically alters reward but not appeal for women *(125)*.

3.6.2.3 Abuse liability of emerging flavoured products

The investigations of the abuse liability of emerging tobacco and nicotine products, including nicotine pouch products and HTP are limited mainly to studies by the tobacco and nicotine industry, very few of which addressed differences by flavour. In most of the industry studies on nicotine pouches, nicotine concentrations were compared for single flavours and not for differences by flavour *(126–130)*. A single non-industry study addressed the abuse liability of nicotine pouches; however, only one flavour type was studied (wintergreen), limiting inferences on the impact of flavours on abuse liability *(131)*. There is also limited evidence on how the appeal or abuse liability of flavours in nicotine pouches compares with that of other tobacco and nicotine products. Comparisons of the abuse liability of flavours are limited to a single study by the tobacco industry, in which several nicotine pouch flavours (wintergreen, cinnamon, citrus, berry coffee and unflavoured) in products with a 4-mg nicotine concentration were compared with participants' usual brand of cigarettes. No significant differences in nicotine intake were reported among the pouch flavours; only citrus-flavoured pouches resulted in a significantly greater nicotine intake than from cigarettes *(132)*. For HTPs, few non-industry studies include examination of abuse liability by flavour.

3.6.2.4 How the form of nicotine impacts the appeal and abuse liability of flavours

An important consideration when examining the effects of flavour on the abuse liability of tobacco and nicotine products is the interaction of flavour with other features of the products that can alter the sensory experience. For example, in ENDS, this could include the form of nicotine (e.g. salt, free base) and features of the product device (e.g. voltage, temperature), which can influence the content and volume of the aerosol and how much nicotine is delivered. Some ENDS devices allow different levels of electrical power, which can affect the e-cigarette

use experience. It has been found that power moderates the positive effects of menthol on appeal, the effects of menthol being larger in low- than in high-power e-cigarette products *(133)*. The form of nicotine has also been shown to alter appeal, such that nicotine salt may enhance the appeal of ENDS more than freebase nicotine *(134,135)*, although its impact on flavour perception is not well studied. Other product features that may impact flavour are synthetic nicotine, which has gained popularity in recent years, and nicotine analogues, which are similar in structure to nicotine and have emerged as an alternative to nicotine products, often to circumvent regulations. Some data indicate that synthetic nicotine alters the taste of ENDS and may be linked to increased e-cigarette use *(136)*, although the role of flavours in synthetic nicotine products and how they compare with flavours in non-synthetic nicotine products is unclear. Little is known about how nicotine analogues affect flavour and appeal, and more work on both these products is necessary to understand how flavour can be manipulated in these products to sustain behaviour.

3.7 Regulation of flavoured products

As of December 2024, more than 50 countries had regional, national or sub-national regulations on additives in tobacco and nicotine products. Most of the regulations address flavouring additives, including bans on the sale, import and manufacture of tobacco and nicotine products with characterizing flavours. Regulations on flavouring additives in tobacco and nicotine products are summarized in Table 3.1. As discussed earlier, the regulations may differ in the definitions of flavours. Some (e.g. EU, USA) differ in the definition of the term "characterizing flavours", which alter the taste or aroma of a tobacco product, while others (e.g. Brazil, Canada) include any additive that is classified as a flavouring agent. Some countries, such as those in the Gulf Cooperation Council (GCC), ban additives by name, while others (e.g. Mauritania) ban additives that enhance palatability or taste as well as the aroma of tobacco and nicotine products. While sugars are not classified as flavours, they also influence the flavour of tobacco products and are therefore also explicitly prohibited as an additive in four countries (Brazil, Cabo Verde, Canada and Netherlands (Kingdom of the) [ENDS only]), although some (e.g. Brazil) permit replacement of sugar lost during curing *(137)*.

Current global regulations can be classified into three categories *(137)*:

- Packaging and labelling regulations: These regulations prohibit the mention of or reference to, through text or images, flavours or foods on packaging, without necessarily banning use of the flavour additives in tobacco and nicotine products. They require manufacturers to change their packaging and to ensure that importers bring in only compliant products, particularly when manufacturing is not local. Kiribati is an example of a country that has adopted this type of policy.

- Sales bans: These regulations prohibit retail outlets from selling products that contain additives, primarily characterizing flavours. The restrictions are directed at distributors and POS rather than manufacturers, so that the additives can still be included in nicotine or tobacco products. This type of regulation is used in the Canadian provinces of Alberta and Nova Scotia and in several cities and states in the USA.
- Tobacco and nicotine product design regulations: Such regulations restrict or prohibit addition of certain additives during the manufacture of nicotine or tobacco products. They regulate manufacturers' production practices and importers to ensure that only compliant products are brought onto the market. Brazil, Canada, the EU and the USA are examples of countries and regions that implement this type of policy.

Regulations on tobacco and nicotine product design can be classified into three categories (Table 3.2):

- Function-focused policies regulate use of additives according to their function, regardless of the amounts used. For instance, Brazil and Canada prohibit additives classified by the Joint FAO/WHO Expert Committee on Food Additives and the FEMA as flavouring agents, regardless of their concentrations *(5,6)*. Thus, additives at levels that may be imperceptible to consumers are also banned.
- Sensory-focused policies regulate additives that have clearly noticeable smells or tastes that differ from those of tobacco before or during consumption, such as fruit, menthol and vanilla flavours. For example, the EU Tobacco Products Directive *(138)* prohibits use of menthol in quantities that would make the product taste distinctly menthol-flavoured and bans use of additives that facilitate inhalation. Use of menthol at concentrations below perceptible levels (approximately 160 ppm) *(139)* have been used to circumvent the prohibition, as observed in Denmark *(140)*.
- Policies focused on health concerns include restrictions on additives known to be harmful to health, particularly those with carcinogenic, mutagenic or teratogenic (CMR) properties, even before combustion. This category includes policies on additives that enhance nicotine uptake. EU member states, members of the GCC and Uruguay have adopted regulations of this nature.

The types of tobacco and nicotine products covered by policies on additives depend on a country's definition of a tobacco product or inclusion of a nicotine or related product. ENDS and ENNDS are included in some policies but are occasionally

explicitly exempted. Similarly, some policies exclude or explicitly include cigars, cigarillos, loose tobacco for roll-your-own cigarettes, waterpipe tobacco and smokeless tobacco products.

Menthol is one of the most commonly used additives in tobacco products *(82)*. Initially, it was not included in all policies; in some cases, it was explicitly excluded, for instance in cigarettes in the USA. Several countries that initially exempted menthol later enacted policies to ban its use (e.g. Canada) *(82,141)*. Flavouring capsules and other flavour accessories are sometimes included in regulations. Exemptions for certain types of products in flavour policies present a challenge, as young people who are attracted to flavoured tobacco products may begin tobacco use with exempted flavoured products. Experience in several countries indicates that exemptions for menthol (Table 3.2) or exclusion of non-cigarette products can undermine public health goals, as some users of flavoured tobacco may switch to menthol, while others may opt for non-cigarette flavoured products *(141–147)*.

A growing, largely unregulated market offers alternative means for delivering flavours in tobacco and nicotine products. They include items such as flavour capsules, beads, flavoured tips, flavoured sprays, flavoured paper and other additives, collectively referred to as "flavour accessories". As these accessories are often not covered in flavour-related regulations, they create additional challenges and loopholes in policy implementation and enforcement, ultimately harming public health *(148,149)*. Implementation of policies on additives in tobacco and nicotine products can be complex, especially in low- and middle-income countries. The tobacco industry is known to oppose policies on additives *(141,150–156)* and has frequently resorted to threats of litigation. In some cases, such policies have even been reversed by government decisions (e.g. in Iran (Islamic Republic of)) *(157)*. Few studies have addressed the potential risk posed by an illegal or black market in response to regulations on flavours. Illegal sale of tobacco products online has been detected in response to tobacco product regulations *(158)*. For example, in California, USA, online shopping and queries about flavoured tobacco products increased significantly after flavour restrictions (Senate bill 793) in 2022 *(159,160)*. Similarly, illegally sold cigarettes have been found in several studies in low- and middle-income countries *(42,161)*, although it is not clear how this is related to flavour restrictions. An assessment of hypothetical purchasing showed that an illegal marketplace will increase purchases of flavoured products after flavour bans *(162)*. It is therefore important to enforce flavour bans strongly and to enact measures to control illegal products, including their marketing channels.

Table 3.1. Regulations on tobacco and nicotine products additives and/or flavours

Country or region	National level (year of implementation)	Sub-national level (year of implementation)
Albania	(2019) Banned placement on the market of tobacco products with characterizing flavours, including menthol *(163)*	*N/A*
Antigua and Barbuda	(2018) Banned tobacco products with a characterizing flavour, containing a flavouring in any component or any technical feature allowing modification of the smell or taste of the tobacco product, or its smoke intensity, including menthol *(164)*	N/A
Australia	(2024) Banned inclusion of prohibited tobacco product accessories (e.g. flavour capsules), including those that alter, or are capable of altering, the flavour or smell of a tobacco product *(165)* (2024) Banned importation of disposable vapes (with and without nicotine); vapes (therapeutic) must be sold only in pharmacies; flavours are limited to mint, menthol and tobacco *(166,167)*	(2017) Queensland: Ban sales of fruit- and confectionery-flavoured tobacco products *(168)* (2018) Western Australia: Packages cannot be displayed by retailers if they contain (or have words, pictures or images that suggest they contain) fruit- or confectionery-flavoured cigarettes; fruit- and confectionery-flavoured cigarettes are prohibited *(169)*. (2012) Tasmania: Sales of fruit- and confectionery-flavoured tobacco products and non-tobacco products (designed to resemble a tobacco product) are prohibited *(170)*. (2009) Victoria: The Secretary may recommend a ban in respect of a product if the product or its smoke possesses a distinctive fruity, sweet or confectionery-like character or the product has packaging that appeals to children or young people *(171)*. Non-tobacco products that resemble a tobacco product or are of a nature or are advertised in a way that may encourage children or young people to smoke and supply of the product should be prohibited, with regard to the objects of the Act. (2008) New South Wales: The Minister may declare a tobacco product prohibited if the product or its smoke has a distinctive fruity, sweet or confectionery-like character that might encourage a minor to smoke *(172)* . (2006) South Australia: The Minister may declare a tobacco product prohibited if the product or its smoke has a distinctive fruity, sweet or confectionery-like character that might encourage a minor to smoke *(173)*.
Bermuda	(2015) Banned the sale of flavoured tobacco products, except with menthol *(174)*	N/A
Brazil	(2012) Banned tobacco additives that alter the flavour and aroma of smoke in all tobacco and non-tobacco products. (Because of court injunctions, several such products remain 0n the market) *(5,150)*.	N/A
Cabo Verde	(2022) Banned tobacco additives that alter the flavour and aroma of smoke in all tobacco and non-tobacco products *(175)*.	*N/A*

Country or region	National level (year of implementation)	Sub-national level (year of implementation)
Canada	(2009) Banned additives (2017) Banned menthol (2018) Banned flavour illustrations on vaping products. Regulation applied to cigarettes, cigars (< 6 g), little cigars, blunt wraps *(6)*	(2010, updated in 2019/2020) Saskatchewan: Banned the sale of flavoured tobacco products and vapour products *(176)* (2015) Nova Scotia: Banned the sale of flavoured tobacco and vaping products *(177)* (2015) Alberta: Banned the sale of flavoured tobacco and vaping products *(178)* (2016) Ontario: Banned the sale of flavoured tobacco products *(179)* (2017) Newfoundland and Labrador: Banned the sale of flavoured tobacco products *(180)* (2020) Northwest Territories: Banned the sale of flavoured tobacco and vaping products *(181)*. (2016/2023) Quebec: Banned the sale of flavoured tobacco products and vaping products (2023) *(182)* (2016/2021) New Brunswick: Prohibition of the sale of all flavoured tobacco (2016) and e-cigarettes (2021) *(183)* (2017) Prince Edward Island: Banned the sale of flavoured tobacco and vaping products *(184)* (2020) Yukon: Banned the sale of flavoured tobacco and vaping products *(185)*
China	(2022) Banned all characterizing flavours (including menthol) other than tobacco in electronic cigarettes. E-cigarette products that do not contain nicotine must not enter the market for sale *(186,187)*. (No date announced) Hong Kong Health Bureau announced that it will ban flavoured cigarettes, including menthol cigarettes and candy- or fruit-flavoured cigarettes *(188)*.	N/A
Congo	(2022) Banned the manufacture, import, distribution, possession, sale or giveaway of flavour capsule cigarettes, cigarettes with characterizing flavours and hookah *(189)*	N/A
GCC (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, United Arab, Emirates)	(2014) prohibited the following additives: Acidum agaricinicum, Oleum betulae empyreumaticum, bitter almond oil associated with or containing hydrocyanic acid, Oleum sassafras, Oleum juniperi empyreumaticum, Oleum camphorae, camphor, coumarin, safrole and thujone. Banned aromas and flavours produced from: Stipites dulcamarae, Lignum camphorae, Rhizoma polypodii, Rhizoma filicis dulcis, Herba pulegii, Lignum quassiae, Cortex quilaiae, Herba tanaceti, Herba rutae, Lignum sassafras, Folia sassafras, Cortex sassafras, Melilotus officinalis, Semen toncae, Liatris odorata, Asperula odorata. Adopted a positive list of additives *(190)*. (2022) Saudi Arabia – some e-cigarette flavours, like cocoa, vanilla, coffee, tea, spices, candy, chewing gum, cola, and alcohol were banned. Fruit flavours, menthol, or a mixture of these are allowed *(191,192)*.	N/A

Country or region	National level (year of implementation)	Sub-national level (year of implementation)
Ethiopia	(2015) Banned flavours, including menthol *(193)*.	N/A
European Union *(92)* (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands (Kingdom of the), Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden)	Banned flavour additives in cigarettes, rolling tobacco and capsules in the European Tobacco Products Directive (2014/40/EU). Menthol banned in 2020. Adopted by all EU members *(138,194)*. (2022) European Tobacco Products Directive requires member states to ban characterizing flavours in HTP *(10,194)*. The following countries have, or had, regulations in addition to the European Tobacco Products Directive: Belgium (2012) banned three ingredients (E418 gomme gellane, E133 "bleu brillant FCF", medium-chain triglycerides used to include "menthol capsules" in cigarettes. Banned TRPM-8 receptor agonists *(195)*. France (2009) established a maximum limit for the presence of: vanilla, vanilline and ethylvanilline in cigarettes. Banned the sweetener applied to the cuff of cigarettes (threshold of analytical detection) *(196)*. Finland (2017) banned all e-liquids with characterizing flavours; therefore, the only permitted flavour is tobacco *(197)*. Germany (2012) banned flavour capsules; (1977, updated in 2016) was the first country to ban additives, in this case additives with CMR properties *(198–200)* Netherlands (Kingdom of the) (2023) banned flavours in electronic cigarettes *(201)* (2025) and banned functional additives, sugars, additives with colouring properties for emissions, additives that facilitate inhalation or nicotine uptake, including TRPM8 receptor agonists, menthol (and derivates) and synthetic coolants in e-cigs and vapes *(202)*. Lithuania: (2009, replaced in 2016 by European Tobacco Products Directive): prohibited CMR additives *(203)*.	N/A
Iran (Islamic Republic of)	(2015) "The use of pictures, flavour or taste of any tobacco products in the production of food and vice versa are banned" *(204)*.	N/A
Kiribati[a]	(2013) Prohibited misleading labelling, including any brand element or any other written terms, descriptor, symbol or sign that directly or indirectly creates the false impression that a particular tobacco product is less harmful than other tobacco products *(205)*.	N/A
Mauritania	(2018) Prohibited use of ingredients that can improve the taste of tobacco products, ingredients that have colouring properties in tobacco products. Menthol is banned *(206)*.	N/A
Mauritius	(2022) Banned the sale, offer for sale, import, manufacture or distribution of tobacco products, including cigarettes that have a characterizing flavour. Menthol is banned *(207)*.	N/A

Country or region	National level (year of implementation)	Sub-national level (year of implementation)
Montenegro	(2019) Prohibited production and marketing of tobacco products with characteristic aroma and aromatic, substances or some technical features that allow change of odour or taste of tobacco product or intensity of tobacco smoke and CMR additives. Menthol is banned *(208)*.	N/A
Niger	(2017) Regulated specified contents of cigarettes, including banning sugars and sweeteners; mint and spearmint; spices and herbs; and other flavours not previously specified. Menthol is allowed *(209)*.	N/A
Nigeria	(2018) Banned characterizing flavours in the manufacture of cigarettes. Menthol is banned *(210)*.	N/A
Norway	(2017) Banned cigarettes and roll-your-own tobacco with a "characteristic flavouring", defined as discernible odour or flavour other than tobacco, as a result of an additive or a combination of additives, such as fruit, spices, herbs, alcohol, candy, menthol or vanilla, and that is noticeable before or during consumption of the goods. This provision will go into effect at a date to be determined by the King *(211)*.	N/A
Philippines	(2022) Prohibited flavours in e-liquids, except menthol and tobacco. Banned flavour descriptors and images on vaporized nicotine or non-nicotine and novel tobacco products *(212)*.	N/A
Republic of Moldova	(2015) Banned tobacco products with characteristic flavour, ingredients that have colouring properties and CMR additives, including menthol *(8)*.	N/A
Senegal	(2016) Banned tobacco products with characterizing flavours. Menthol is banned *(213)*.	N/A
Sierra Leone	(2022) Banned the manufacture, import, distribution and offer for sale of tobacco or nicotine products with characterizing flavours and additives associated with increased nicotine uptake *(214)*.	N/A
Sri Lanka	(2016) Banned the manufacture, import, sales or offer for sale of any smokeless tobacco product or mixture that contains tobacco; any flavoured, coloured or sweetened cigarette that contains tobacco; any electronic cigarette that contains tobacco. Menthol is banned *(215)*.	N/A
Türkiye	(2019) Banned the sale of cigarettes and crushed rolling tobacco with characterizing flavour. Banned tobacco products containing additives with colouring properties for emissions that make inhalation or nicotine delivery easier for smoking tobacco and CMR properties in unburnt form. Menthol is banned *(9)*.	N/A
Ukraine	(2021) Banned tobacco products with a characteristic smell and/or taste, additives that can colour emissions, additives with CMR properties in unburnt form and additives that facilitate nicotine uptake or the inhalation of smoke. Menthol is banned *(216)*.	N/A
Uganda	(2015) Banned flavoured tobacco products, tobacco products with any technical feature that allows the release or modification of the smell or taste of the tobacco product or the smoke intensity, that contains colouring properties for emissions, and that has flavour-delivering mechanisms including filter flavour capsules, granules and flavour threads *(217)*.	N/A

Country or region	National level (year of implementation)	Sub-national level (year of implementation)
United Kingdom	(2016) Banned cigarettes and hand-rolling tobacco with a characterizing flavour, other than menthol, with colouring effects on emissions, that facilitate inhalation or nicotine uptake, additives with CMR properties in unburnt form or when consumed *(218)*. (2020) Banned menthol *(219)*.	N/A
USA[b]	(2009) Banned additives or ingredients that impart characterizing flavour to the tobacco product or tobacco smoke in cigarettes and roll-your-own tobacco; exempts menthol *(7)*. (2022) Proposed rule to prohibit menthol in cigarettes and to prohibit all characterizing flavours (other than tobacco) in cigars *(143)*.	(2022) California: Sale of most flavoured tobacco products prohibited: 143 municipalities and counties regulate additives. Menthol is banned in the state *(220–222)*. Colorado: 7 municipalities and counties regulate additives. Menthol is banned in 6 municipalities and counties *(220–222)*. Georgia: 1 municipality or county regulates additives. Menthol is banned in 1 municipality or county *(220–222)*. Illinois: 4 municipalities or counties regulate additives. Menthol is banned in 1 municipality or county *(220–222)*. Maine: 8 municipalities or counties regulate additives. Menthol is banned in 7 municipalities or counties *(220–222)*. (2020) Maryland – Flavoured e-cigs were banned – 1 municipality has additive regulations. Menthol is banned *(220–222)*. (2019) Massachusetts: Sale of all flavoured tobacco products is banned. Menthol is banned at state level. 168 municipalities or counties regulate additives. Menthol is also banned in 22 municipalities or counties *(220–222)*. Minnesota: 30 municipalities/ counties regulate additives. Menthol is banned in 22 municipalities or counties *(220–222)*. (2019) Montana – temporary ban of flavoured e-cigs in response to EVALI no longer in force. 1 municipality or county regulates additives. Menthol is banned in 1 municipality or county *(220–222)*. (2018) New Jersey: Sale of all flavoured e-cigarettes prohibited in all locations. Menthol is banned at state level. 4 municipalities or counties regulate additives *(220–222)*. (2019) New York: Sale of all flavoured e-cigarettes is banned in all locations. Menthol is banned at state level: 2 municipalities or counties regulate additives *(220–222)*. North Dakota: 2 municipalities or counties regulate additives. Menthol is allowed *(220–222)*.

Country or region	National level (year of implementation)	Sub-national level (year of implementation)
		Ohio: 3 municipalities or counties regulate additives. Menthol is banned in 2 municipalities or counties *(220–222)*. Oregon: 2 municipalities or counties regulate additives. Menthol is banned in 2 municipalities or counties *(220–222)*. (2020) Rhode Island: Sale of all flavoured (including menthol) e-cigarettes prohibited in all locations: 6 municipalities or counties regulate additives *(220–222)*. (2021) Washington DC: Sale of flavoured tobacco products (not applied to flavoured hookah consumed on site), including e-cigarettes, prohibited. Menthol is banned *(220–222)*. (2020) Utah: Sale of flavoured e-cigarettes is banned. Menthol is allowed *(220–222)*.
Uruguay	(2008) Banned ammonia in tobacco products. Menthol and other additives and flavours are allowed *(223)*.	N/A

Source: updated from El-Hellani et al. *(1)*
N/A, not applicable
[a] Countries that regulated only messages about additives or flavours on packaging. No regulations were found on the use of flavours or additives in tobacco products.
[b] For updated information on the regulatory status of cities in the USA, see *7,220*.

Table 3.2. Regulations on additives and inclusion or exclusion of menthol by type of policy and country

	Type of regulation					
			Product design			
Country	Packaging and labelling	Sales ban	Sensorial	Functional	Health concerns	Exemption of menthol
Albania	No	No	Yes		No	No
Antigua and Barbuda	No	No	No	Yes	No	No
Australia	No	Yes	Yes	No	No	No / Yes (e–cigarettes exempted)
Bermuda	No	No	Yes	No	No	Yes
Brazil	No	No	No	Yes	No	No
Cabo Verde	No	No	No	Yes	No	No
Canada	No	Yes	No	Yes	No	No
China	No	No	Yes	No	No	Yes
Congo	No	No	Yes	No	No	No
GCC (6 countries)	No	No	Yes (Saudi Arabia)	No	Yes (CMR)	Yes
Ethiopia	No	No	Yes	No	No	No
EU (27 countries)	No	No	Yes	Yes (Netherlands, Kingdom of the)	Yes (CMR and nicotine uptake)	No
Iran, Islamic Republic of	No	No	Yes (no longer in force)	No	No	Yes

Country	Type of regulation					
	Packaging and labelling	Sales ban	Product design		Health concerns	Exemption of menthol
			Sensorial	Functional		
Kiribati	Yes	No	No	No	No	Yes
Mauritania	No	No	No	Yes	No	
Mauritius	No	No	Yes	No	No	No
Montenegro	No	No	Yes	No	Yes (CMR and nicotine uptake)	No
Niger	No	No	Yes	No	No	Yes
Nigeria	No	No	Yes	No	No	No
Norway	No	No	Yes (not in force)	No	No	Yes
Philippines	Yes	No	Yes	No	No	Yes
Republic of Moldova	No	No	Yes	No	Yes (CMR and nicotine uptake)	No
Senegal	No	No	Yes	No	No	No
Sierra Leone	No	No	Yes	No	Yes (nicotine uptake)	No
Sri Lanka	No	No	Yes	No	No	No
Türkiye	No	No	Yes	No	Yes (CMR and nicotine uptake)	No
Ukraine	No	No	Yes	No	Yes (CMR and nicotine uptake)	No
Uganda	No	No	Yes	No	No	No
United Kingdom	No	No	Yes	No	Yes (CMR and nicotine uptake)	No
USA	No	Yes	Yes	No	No	Yes (only in certain jurisdictions)
Uruguay	No	No	No	Yes (only ammonia)	Yes (nicotine uptake)	No

Source: updated from El-Hellani et al. *(1)*

3.7.1 Case study: Netherlands (Kingdom of the)

Netherlands (Kingdom of the) has a long history of tobacco control, beginning in 1957 with the Health Council's report "Smoking and Health", which highlighted the link between smoking and lung cancer. This prompted health organizations such as the Dutch Cancer Society to act. In 2023, the country became the fourth, after Brazil, Mauritius and Türkiye, to implement the six MPOWER measures *(224)* at the highest level to reduce demand for tobacco effectively.

The long history of tobacco control has been extended to regulation of additives in tobacco and nicotine products. In addition to the restrictions prescribed by the European Union, such as the ban on cigarettes and HTP with "characterizing flavours", including menthol, Netherlands applied additional legislation to electronic cigarettes on 1 April 2025, prohibiting flavour-determining additives as constituents of nicotine-containing and non-nicotine-containing e-liquids and other components. The list of banned substances includes vitamins,

amino acids, minerals and substances that create the impression of health benefits, including caffeine, taurine, guarana, other stimulant and stimulating mixtures associated with energy and vitality, eugenol, extracts of tea, sugars, agents with colouring properties and additives that facilitate inhalation or promote nicotine uptake (such as TRPM-8 receptor agonists, menthol) *(202)*.

Additionally, Netherlands, through the National Institute for Public Health and the Environment, engages in research, offers technical support and develops materials related to flavour additives in tobacco and nicotine products. This work significantly promotes both national and international policies.

More information on aspects of tobacco control in Netherlands is available from:

- Prevalence of smoking – (https://www.cbs.nl/en-gb/figures/detail/85457ENG)
- Flavouring additives in tobacco and nicotine products regulations:
  - Amendment of the Tobacco and Smoking Products Decree in connection with the regulation of flavours for e-cigarettes (https://zoek.officielebekendmakingen.nl/stb-2022-463.pdf);
  - Regulation of the State Secretary for Health, Welfare and Sport of 6 March 2024, reference number 3770816-1061446-WJZ, amending the Tobacco and Tobacco Products Regulation in connection with the establishment of a list of additives prohibited for tobacco products and electronic vapor products (https://zoek.officielebekendmakingen.nl/stcrt-2024-7582.html);
  - Directive 2014/40/EU of the European Parliament and of the Council of 3 April 2014 on the approximation of the laws, regulations and administrative provisions of the Member States concerning the manufacture, presentation and sale of tobacco and related products and repealing Directive 2001/37/EC (https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32014L0040); and
  - Amending Directive 2014/40/EU of the European Parliament and of the Council as regards the withdrawal of certain exemptions in respect of HTP (ban of flavourings in HTP) (https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32022L2100).

3.7.2 Impact of regulation of specific flavoured products

Recent studies indicate that the prohibition of additives has been effective in the locations studied. Most research, however, is on menthol as an additive, primarily because it is easy to identify in both consumed products and users, and menthol is particularly popular among populations of African–American and Hispanic origin in the USA *(78,225)*.

A study conducted in the USA *(226)* indicated that the ban on flavoured cigarettes resulted in a

> significant immediate increase as well as reductions over time in youth and young adult use of any cigarettes and menthol cigarettes, compared to older adults. Specifically, the likelihood of younger smokers continuing to smoke dropped from 43% to 27%.

In contrast, there was no significant change in smoking rates over time among adult smokers. This study suggests that the ban on menthol cigarettes has a stronger impact on children and adolescents *(226)*. The potential impact of a ban on menthol cigarettes in the USA was modelled in a clinical study *(227)*. When cigarette users were asked to switch to non-menthol instead of menthol cigarettes, reductions were observed in both the number of cigarettes smoked and nicotine dependence. The reductions were particularly notable among smokers of Black (versus White or Hispanic) ethnicity.

In Ontario, Canada, after prohibition of flavour and other additives, users of menthol cigarettes, who were usually younger, significantly increased their attempts to quit smoking *(228)*, the quit attempt rate increasing to 24% for regular menthol smokers, 20% for occasional menthol smokers and 14% for non-menthol smokers after 1 year. Another study in Canada *(142)* found that banning additives, particularly menthol, was highly effective in areas with large populations of menthol cigarette smokers. Additional studies in Canada support these findings *(229)*.

A study in New York City, USA, in 2017 showed that prohibiting flavoured tobacco products led to a reduction in tobacco consumption among adolescents *(230)*. Similarly, in a study among Dutch smokers *(231)*, a decrease in the number of menthol cigarette smokers and an increase in quit attempts were observed after the European ban on additives. In England, after the ban on sales of menthol cigarettes *(145)*, younger individuals significantly reduced use of these products.

In summary, bans on flavoured additives appear to impact smoking habits among youth more than adults and have been effective in preventing initiation and in encouraging cessation among children and young adults. There is increasing evidence that policies on additives in cigarettes effectively prevent youth from starting to use tobacco products and support those trying to quit. It should, however, be noted that the findings are based on data and studies from high-income countries.

Each policy approach has advantages and disadvantages (see Table 3.3). For instance, while "characterizing flavours" have been banned in certain countries, a significant drawback is the challenge of defining what constitutes or what concentration of additives constitutes a "characterizing flavour". People's perceptions of flavours may differ widely among individuals and populations. Thus,

a tobacco product with a noticeable flavour in one region might be considered unflavoured in another. Most countries that regulate menthol address only perceptible menthol, i.e. menthol as a "characterizing flavour" and not as an additive, so that subliminal menthol is unregulated. For instance, the low levels of menthol that can reduce irritation and alter the taste of tobacco may not be classified as "characterizing flavour" *(139)*. Consequently, policies that address only "characterizing flavours" should be monitored closely, as manufacturers may use other additives or existing ones at lower levels to enhance product appeal and acceptability. This could ultimately impact the public health outcomes associated with these regulations. Regulations based on functional characteristics could, however, be technically challenging and might face stronger opposition from tobacco companies. Countries should nevertheless consider that, regardless of the policy on flavour additives adopted, their effective implementation and enforcement will contribute to reducing tobacco and nicotine use, especially among younger people.

Table 3.3. Advantages and disadvantages of different policies on tobacco product additives

Policy type[a]		Advantages	Disadvantages	Comments
Sales ban		Adaptable to local circumstances Easily understood by the public Easy to implement Low cost of implementation	Limited scope when only applied to products with characterizing flavours and explicit mention of the flavour	Exceptions (products and additives) create loopholes when flavoured products remain available Evidence of effectiveness at local level *(227,232)*.
Labelling		Easy to implement Low implementation cost	Does not interfere with product flavour Allows use of additives and flavours	Can strengthen other regulatory policies on additives or flavours if combined No evidence of effectiveness
Tobacco product design	Functional	Comprehensive if all products are included Prevents use of additives that make tobacco products more palatable or acceptable, regardless of the perception of the user.	Demands highly qualified human resources for enforcement Time to implementation might be longer Additives that change flavour can be described as having a different function to avoid compliance	Can be applied to prevent use of additives that make tobacco products more palatable and use of flavoured products Enforcement might be facilitated if policy includes all additives and all products Evidence of effectiveness (Canada) *(142,144,228,229)*
	Sensorial	Easy to implement if evidence of characterizing flavour is readily available Low implementation cost Easily understandable to the population	Allows use of additives at levels that are not perceived by the consumer or branding Enforcement requires highly qualified workforce and laboratory facilities	The most common regulatory approach Enforcement might be facilitated by establishment of an independent advisory panel on the presence of characterizing flavours Evidence of effectiveness (EU and USA) *(139,140,147,228)*

Reproduced from El-Hellani et al. *(1)*

[a] Regulations that address health concerns are not included.

3.8 Discussion

Use of flavours in tobacco and nicotine products raises complex issues. Flavours appeal to youth and young adults and may enhance abuse liability and use of tobacco and nicotine products. The presence of flavours in products such as e-cigarettes and nicotine pouches has also been reported to enhance their appeal and thus increase their acceptability by users of smoked tobacco who may be trying to quit. While there is some evidence that certain flavour additives contribute to the toxicity of tobacco products, more evidence is necessary. Additionally, in emerging products, non-traditional additives (e.g. synthetic coolants that do not impart a traditional "taste" but still alter sensory perceptions) may be used to enhance flavour, with use of concept flavour names in marketing. Regulation varies globally, some countries applying comprehensive flavour regulations and others regulating each product. Policy-makers should consider how new additives and new product types can be included in existing regulations to limit the spread of tobacco and nicotine use, especially among youth and tobacco-naive populations.

To address the different political contexts in countries, the opposition of the tobacco and nicotine industries to such measures and the technical capacity and legal framework of each country, a comprehensive ban on product design might help to decrease the attractiveness of tobacco and nicotine products. This could lead to a reduction in initiation and in nicotine dependence among users. Claims of harm reduction or therapeutic purposes should not exempt countries from applying policies to control flavour additives. If more restrictive policies cannot be implemented, a country should monitor use of tobacco and nicotine products and select the most suitable regulatory model and the range of products to be considered. Monitoring will also allow countries to keep track of new tobacco and nicotine products and to update regulations as necessary. A recent example is nicotine pouches, which are available in a range of appealing flavours but remain unregulated in many jurisdictions.

Countries should avoid interference by the tobacco and nicotine industries in formulating their policies on flavour additives in these products. They should also work towards harmonizing definitions of flavours and constituents. A piecemeal approach to regulating flavoured tobacco and nicotine products will not turn the tide of the tobacco epidemic. A multi-pronged combination of various policy tools, with a panoramic view of all tobacco and nicotine product use, will help health agencies to address the issue of flavoured products *(1–3,142,232)*.

3.9 Research gaps, priorities and questions

Research is necessary to support regulatory action on the following aspects of flavoured tobacco and nicotine products, especially ENDS, nicotine pouches and HTPs, and development of global regulations to reduce use of flavoured tobacco products.

- Conduct surveillance of the global epidemiology of use of flavoured tobacco and nicotine products.
- Conduct longitudinal studies of use of emerging tobacco and nicotine products, including nicotine pouches, and the role of flavours in initiation, uptake and continued use.
- Develop consensus on a definition of a "flavouring agent", and ensure inclusion of "odourless" additives, such as synthetic coolants, and the relevant terminology.
- Understand the impact of synthetic coolants and other emerging synthetic flavours on the appeal, abuse liability and toxicity of tobacco and nicotine products.
- Further examine the impact of flavour on the experience of tobacco and nicotine reward, by age group and tobacco use status.
- Study the short- and long-term toxicity of flavour ingredients in tobacco and nicotine products.
- Study the role of flavours in changing from smoked to other tobacco and nicotine products by people who smoke.
- Analyse the impact of global regulations, restrictions and bans on flavours in new and emerging tobacco and nicotine products, especially nicotine products, including by modelling responses to flavour-related policies and their impact on abuse liability in hypothetical scenarios and tasks.

Global priorities are to:

- build evidence of the impact of flavours on use of tobacco and nicotine products by age group and on the use of different products in different countries;
- determine the impact of flavours in tobacco and nicotine products on the decades-long effort to reduce tobacco and nicotine use in the population;
- understand establishment of country-specific, comprehensive regulations on flavours in tobacco and nicotine products, and enforce those regulations; and
- encourage communication among countries on their experience with regulation of flavours in tobacco products.

Questions to be posed to policy-makers and international organizations such as WHO include the following.

- How can concern about the use of flavours and additives in tobacco and nicotine products, specifically emerging nicotine and tobacco

products such as nicotine pouches and HTP, be addressed rapidly to prevent a new generation of users from becoming dependent on tobacco and nicotine?

- What can be done to outpace industry manoeuvres to avoid regulation, such as use of synthetic coolants to enhance the appeal and use of their products?
- Can a robust, self-developing, sustainable regulatory model be built to address similar concerns about any new or modified tobacco product?

3.10 Recommendations

To reduce the appeal of tobacco and nicotine products, countries should consider the following measures and enforce them strictly.

1) Comprehensively ban all flavours (except tobacco flavours) in all tobacco, nicotine and related products, including flavour accessories, to make them less attractive and appealing, especially to children and young people.
2) Implement a comprehensive ban, covering all media, including the Internet and social media, on marketing of tobacco, nicotine and related products and all forms of promotion that depict, reference or suggest flavours.
3) If a complete ban is not feasible or indicated, subject flavouring chemicals or agents to strict regulation and monitoring, both in their use as product constituents and in all forms of marketing.
4) Ensure that the legal definition of "flavours" is broad, comprehensive and future-proof and that it covers synthetic, analogue and any other substance or combination thereof that impart a sensory effect, in order to prevent industry exploitation of regulatory loopholes.
5) Engage all relevant authorities, including in health, trade, customs, education, consumer protection and law enforcement, in the design, implementation and monitoring of flavour-related measures to ensure comprehensive enforcement and to address cross-sectoral challenges.
6) Continuously monitor the market for new flavour-related innovations, synthetic additives or product designs intended to circumvent flavour bans, and update regulations accordingly.

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4. Science of sugars in tobacco and nicotine products and regulatory recommendations, an update

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Contents

Abstract
4.1 Background
4.2 Methods
4.3 Sources and levels of sugars in tobacco and nicotine products
  4.3.1 Types of sugars naturally present in tobacco and the impact of processing
  4.3.2 Sugars and sweeteners added during processing
  4.3.3 Methods for measuring sugars and sweeteners in tobacco and nicotine products
  4.3.4 Types and levels of sugars in various tobacco and nicotine products
    4.3.4.1 Smoked products
    4.3.4.2 Smokeless tobacco
    4.3.4.3 E-cigarettes and heated tobacco products
    4.3.4.4 Nicotine pouches
4.4 Chemistry of the thermal degradation of sugars and sweeteners
4.5 Contribution of sugars to the abuse liability of tobacco and nicotine products
  4.5.1 Contribution of sugars to the attractiveness of tobacco and nicotine products
  4.5.2 Contribution of sugars to the addictiveness of tobacco and nicotine products
    4.5.2.1 Effects on the bioavailability of nicotine in product emissions
    4.5.2.2 Contribution to the addictive properties of nicotine
4.6 Implications of sugars and sweeteners for the toxicity of tobacco and nicotine products
  4.6.1 Contribution of sugars and sweeteners to toxic emissions from various tobacco and nicotine products
    4.6.1.1 Contribution of sugars to cigarette smoke emissions
    4.6.1.2 Contribution of sugars and sweeteners to waterpipe tobacco smoke emissions
    4.6.1.3 Contribution of sugars and sweeteners to e-cigarette emissions
    4.6.1.4 Contribution of sugars and sweeteners to heated tobacco product emissions
  4.6.2 Implications of toxicity for people who smoke or use heated tobacco and nicotine products
  4.6.3 Implications of toxicity for people who use smokeless tobacco and nicotine products
4.7 Effects of sugars on perception and use of tobacco and nicotine products
4.8 Tobacco industry research on sugars in tobacco products
  4.8.1 Industry approach to testing the toxicity of ingredients
  4.8.2 Findings of industry research on toxicity
  4.8.3 Limitations of industry research on toxicity
  4.8.4 Exploration or use of alternatives to sugars by the industry
4.9 Regulation of sugars

4.9.1. Examples of relevant regulation of tobacco and nicotine products
4.9.2 Challenges associated with regulating sugars in tobacco and nicotine products
4.10 Summary and conclusions
4.11 Areas for research and future directions
4.12 Policy recommendations
References

Abstract

Sugars and sweeteners in tobacco and nicotine products have a profound impact on product palatability and may contribute – directly or indirectly – to product addictiveness and toxicity. This paper updates previous reviews by the WHO TobReg. It summarizes published evidence on the presence and the effects of sugars in various tobacco and nicotine products and reviews tobacco industry research on this topic. Our main conclusions are that (i) sugars and/or sweeteners are present in all tobacco and nicotine product categories that have been analysed for these ingredients, albeit at various levels; (ii) there is strong evidence that sugars and sweeteners contribute to the attractiveness of tobacco and nicotine products; (iii) there is accumulating evidence of the contribution of sugars and sweeteners to the toxic emissions of smoked and heated products; (iv) there is accumulating evidence of the potential contribution of sweeteners to the addictiveness of tobacco and nicotine products; (v) there is emerging concern about the potential contribution of sugars in tobacco and nicotine products to the risk for oral cancer; and (vi) evidence of continuous efforts by tobacco and nicotine product manufacturers to undermine product regulations, such as on the use of synthetic substitutes for regulated constituents, suggests that regulation of sugars may result in similar interference. The paper provides policy and research recommendations in response to these findings and conclusions.

Keywords: Sugars, sucrose, glucose, fructose, sweeteners, toxic emissions, toxicity, attractiveness, addictiveness

4.1 Background

Articles 9 and 10 of the WHO FCTC are core provisions for demand reduction in the WHO FCTC, which provide a framework for effective regulation of the contents and emissions of tobacco products. The partial guidelines for implementation of Articles 9 and 10 of the WHO FCTC *(1)* propose regulation of tobacco products and disclosures as a measure that may assist Parties in strengthening their tobacco-control policies. Such regulation may involve a range of tobacco demand reduction measures to reduce the attractiveness and addictiveness of tobacco and nicotine products, which can also lead to reductions in toxic exposures from their use. An example is the introduction of product standards on composition, such as

setting limits on certain constituents in the contents and emissions of tobacco and nicotine products and/or prohibiting the use of certain additives in these products. Product standards can contribute directly to reducing the addictiveness, attractiveness and toxicity of tobacco and nicotine products and, as a consequence, to decreasing the morbidity and mortality attributable to their use.

This report addresses sugars and sweeteners in tobacco and nicotine products. Sugars and sugar-containing ingredients (e.g. honey, corn syrup and molasses) are key components of the majority of tobacco products *(2–4)*. In addition, high-intensity sweeteners, which are chemically distinct from sugars but confer a sweet taste, are often found in nicotine-containing products such as electronic cigarettes and nicotine pouches *(5–7)*. Sugars and sweeteners contribute in many ways to the morbidity and mortality associated with the use of tobacco (e.g. cigarettes and smokeless tobacco) and nicotine products (e.g. electronic nicotine delivery systems and nicotine pouches). First, the types and the amounts of sugars and sweeteners in a specific product type or brand are usually tailored by manufacturers to confer certain chemosensory properties (e.g. smoothness, flavour) *(2,3)*. These properties increase product appeal and attractiveness and lower risk perceptions in users and are known to be associated with tobacco and nicotine product uptake and sustained use *(8–10)*. In addition, sugars and some of the products of sugar decomposition can contribute to product addictiveness *(11–14)*. Sugars also contribute to product toxicity, either directly (in smokeless tobacco products) or indirectly, due to thermal decomposition when smoked or heated *(15,16)*. Because of this multidimensional impact on users, regulation of sugars and sweeteners in tobacco and nicotine products is likely to protect public health.

The Seventh Report of the WHO TobReg *(17)* summarized data on the levels and sources of sugars in various types of tobacco products and the effects on product toxicity and abuse liability (attractiveness, addictiveness). The report identified key research gaps, such as on the role of sugars in product addictiveness and their contribution to harmful exposures and health effects in users. The current report reviews the key science of sugars in tobacco and nicotine products and adds research that has been conducted during the past 5 years, including on sweeteners in e-cigarette liquids and nicotine pouches. This document served as a background paper for the Tenth WHO technical report on the scientific basis of tobacco product regulation.

The paper includes an update on the topics covered in the previous reports of the WHO Study Group, particularly the seventh report *(17)* and the ninth report *(18)*, such as the levels of sugars and sweeteners in tobacco and nicotine products and their contribution to product appeal and toxicity. For more complete information on this subject, readers should refer to the information available in the seventh report. Methods for the analysis of sugar in products and an overview of tobacco industry research on sugars are included here. Examples of country

experiences with regulating sugars and other relevant product standards are summarized. We also review gaps in and priorities for research and provide policy recommendations. Specifically, this paper covers:

- sources and levels of sugars in tobacco and nicotine products, including methods for measuring sugar;
- an overview of the contribution of sugars to abuse liability (e.g. attractiveness and addictiveness) and to the toxicity of tobacco and nicotine products;
- studies of the effects of sugar on people who use tobacco and nicotine products;
- tobacco industry research on sugars in tobacco products;
- regulation of sugars: country experiences and considerations;
- research gaps and priorities; and
- policy recommendations.

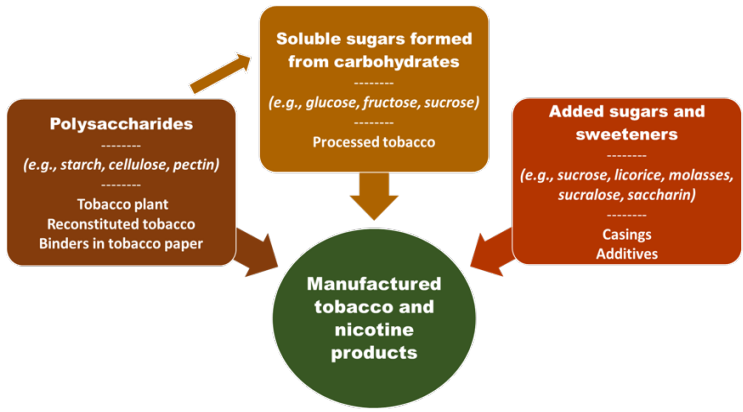
4.2 Methods

A search of the literature was conducted between January and November 2024, with the seventh report *(17)* as the starting point and a search for papers published from 2019. For keywords, we used combinations of the words "sugars" and "sweeteners" with "tobacco", "e-cigarettes" and "nicotine pouches". We primarily used the PubMed database and also relevant articles cited in publications obtained in the database search. In addition, internal tobacco industry documents related to toxicological testing of sugars as tobacco ingredients were identified in the University of California at San Francisco Truth Tobacco Industry Documents collection. We used a "snowballing" search method, wherein a set of initial key terms (e.g. sugar, glucose, fructose, sucrose) was extended with additional keywords that emerged from the review of documents. We also reviewed the websites of various regulatory agencies and other information relevant to country experiences in sugar regulation.

4.3 Sources and levels of sugars in tobacco and nicotine products

The three main sources that contribute to the total content of sugar compounds in a finished tobacco and nicotine product are: polysaccharides (chemically defined as sugars but not imparting a sweet taste) present in tobacco plants and in other components of a product; soluble simple sugars (mono- and disaccharides with a sweet taste, such as glucose, fructose and sucrose) derived from carbohydrates during tobacco processing; and sugars and sweeteners added as casings and additives during product manufacture (Fig. 4.1).

Fig. 4.1. Sources of sugar compounds and sweeteners in tobacco and nicotine products



Below we briefly outline the types and the levels of sugar compounds in various tobacco and nicotine products, focusing on the soluble sugars that are naturally present and added sugars and sweeteners.

4.3.1 Types of sugars naturally present in tobacco and the impact of processing

Up to 30% of the tobacco plant weight is comprised of carbohydrates, including polysaccharides such as starch, cellulose and pectin *(4,18)*. During tobacco processing, such as in the early stages of drying and curing, enzymatic hydrolysis of these carbohydrates produces soluble sugars, the most abundant being fructose and glucose, and smaller amounts of sucrose. The relative levels of such "naturally" present sugars in processed tobacco differ by the main tobacco type. For example, Burley tobacco, which is widely used in cigarette blends in the USA and in some European cigarette varieties, is typically subjected to air-curing, a slow process that does not involve heating and therefore allows sugars to be metabolized enzymatically *(18,19)*. Virginia tobacco is processed by flue-curing at elevated temperatures, which prevents enzymatic degradation of sugars. As a result, processed Burley tobacco may contain < 0.2% of sugars by weight before addition of external sugars, while Virginia tobacco may contain ≤ 30% of sugars after curing *(4,18,19)*.

Several other factors contribute to the overall content of naturally derived sugars in a manufactured tobacco product (Fig. 4.1). For example, blending of different tobacco types can contribute to the variation in soluble sugars among cigarette brands: American-blended cigarettes contain a mixture of Burley and Virginia tobaccos (up to 35% of each) and smaller amounts of other tobaccos, while some cigarettes popular in Europe and other countries may contain a single tobacco type, resulting in either high or low sugar levels *(19)*.

4.3.2 Sugars and sweeteners added during processing

The types of sugars and sweeteners added to tobacco and nicotine products by manufacturers are summarized in Table 4.1.

Table 4.1. Types of sugars, sugar-containing ingredients, sweeteners and sugar substitutes used in various tobacco and nicotine products

Sugar and sugar additive types	Examples of additives	Tobacco and nicotine products that may contain these sugars[a]
Soluble mono- and disaccharides	Sucrose, invert sucrose, dextrose, lactose, maltose	Cigarettes, cigars, smokeless (chewing) tobacco, waterpipe tobacco
Complex sugar-based additives	Liquorice, cocoa, high-fructose corn syrup, honey, molasses, caramel	Cigarettes, smokeless (chewing) tobacco, waterpipe tobacco
Natural non-sugar sweetener additives	Maltol, glycerol, sorbitol, thaumatin	Cigarettes, smokeless tobacco, e-cigarettes, nicotine pouches
Synthetically produced sweetener additives	Sucralose, aspartame, acesulfame-k, saccharin, ethyl maltol, maltitol, propylene glycol, dextrin	Cigarettes, smokeless tobacco, e-cigarettes, nicotine pouches

From references *2–7,15,20*

[a] Other products, such as heated tobacco products, may contain these sugars and sweetener; however, only products for which published data on the presence of corresponding sugars were available are included.

Soluble sugars and sugar-containing additives have long been used by tobacco product manufacturers in tobacco-containing products such as cigarettes, smokeless tobacco and waterpipe tobacco, with the goal of increasing the palatability of tobacco products *(2)*. The typical process of addition of sugars to tobacco is in the form of casings, to compensate for the loss of sugars during tobacco drying and curing and to reduce smoke harshness (see section 4 for more detail). Sucrose, invert sugar (the hydrolysis product of sucrose), high-fructose corn syrup, liquorice and cocoa are among the most frequently used casing materials and are listed as ingredients of the majority of tobacco product brands by manufacturers who disclose product ingredients either on their websites or to regulators. Tobacco manufacturers have also used various other sugar-containing ingredients, such as honey, molasses and fruit juices *(2–4,15)*.

In addition to sugars and sugar-containing ingredients, certain substances with a sweet taste are commonly used in tobacco and nicotine products. They include substances extracted from various plants (e.g. naturally occurring sugar alcohols such as maltol and glycerol) and high-intensity synthetic sweeteners (e.g. sucralose, aspartame) (Table 4.1).

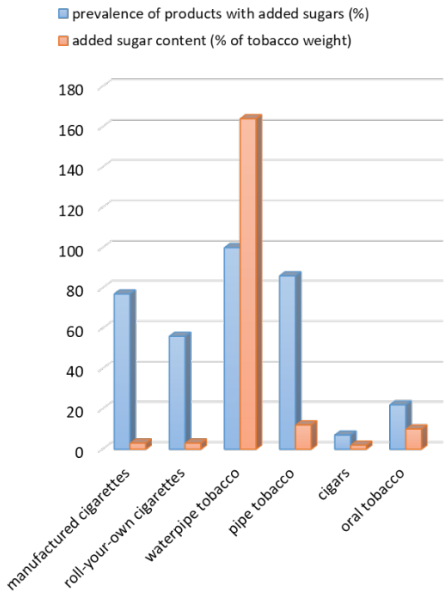
4.3.3 Methods for measuring sugars and sweeteners in tobacco and nicotine products

Sugars in aqueous extracts of tobacco products can be measured by high-performance liquid chromatography coupled with an evaporative light scattering detector *(21)* or with mass spectrometry *(5)*. Mass spectrometry techniques are also used for analysing sweeteners *(22,23)*.

4.3.4 Types and levels of sugars in various tobacco and nicotine products

Overall, there are few reports on the levels of specific sugars and sweeteners in tobacco and nicotine products. Fig. 4.2 summarizes the prevalence of brands with added sugars in various conventional (i.e. tobacco-containing) product types from data the Seventh WHO TobReg report *(17)* and the content of added sugars expressed as a percentage of tobacco weight. Table 4.2 provides examples of published data on soluble sugars (glucose, fructose and sucrose) – which may be either tobacco-derived or additives – in various product types. More recent data on sugars and sweeteners in various tobacco and nicotine products are cited below.

Fig. 4.2. Reported prevalence of products with added sugars in various tobacco product types and the content of added sugars relevant to tobacco weight in each



From WHO *(17)*.

Table 4.2. Levels of commonly reported soluble sugars in various tobacco and nicotine product typesa

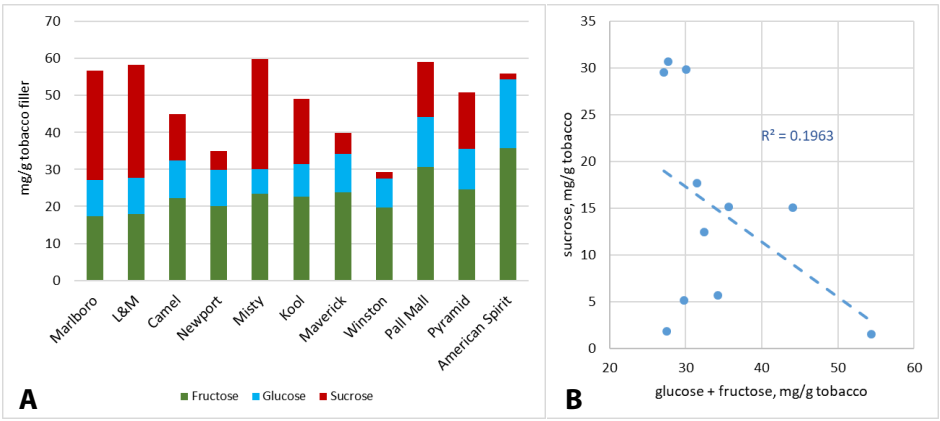
Product type	Glucose	Fructose	Sucrose	Country (year)
				USA (2006, 2017) *(5,23)*
	6.5–33.5	18.2–57.6	5.2–47.2	Netherlands (Kingdom
	16–115	7–63	3–28	of the) (2020) *(21)*
Cigarettes	14.1–106.2	32.2–101.2	4–22.9	China (2007) *(24)*
	0.02–3.5	LODa – 3.2	LOD –3.6	USA (2006) *(23)*
Cigars	0.3	LOD	0.4	China (2007) *(24)*
Snuff	LOD –1.6	LOD –0.2	LOD	USA (2006) *(23)*
Chewing tobacco	LOD –104.3	18.9–209.6	0.26–224.6	USA (2006) *(23)*
Waterpipe tobacco	125–195	135–90	LOD –9	USA (2020) *(25)*
E-cigarette liquids	0.006–0.089	0.009–0.33	0.009–0.62	USA (2018) *(26)*

[a] Levels in all products except for e-cigarette liquids are expressed as mg/g product (converted from % weight in some reports). Levels in e-cigarette liquids are expressed as mg/mL.
LOD, limit of detection

4.3.4.1 Smoked products

Cigarettes. While the typical total amount of sugars in cigarette tobacco is 5–10%, the amount of added sugars differs by brand, and may represent 2–18% of the tobacco filler weight *(5)*. Despite manufacturers' claims that sugars are simply "added back" to tobacco to replace those lost during processing, the variation in the amount of added sugars appears to exceed that of natural sugars. For example, in a recent analysis of 50 popular US cigarette brands, the concentrations of glucose and fructose (which are naturally present in tobacco leaf) varied by approximately four times among brands, while sucrose (usually found in very small amounts in tobacco and thus represents added sugars) differed by more than 55 times (Fig. 4.3A).[1] Even though levels of sucrose are significantly negatively correlated with the sum of glucose and fructose (Fig. 4.3B), the substantial variation in total soluble sugars (e.g. the sum of fructose, glucose and fructose) among brands suggests that manufacturers are not simply replenishing lost sugars but carefully tailoring the total sugar content to achieve specific properties of cigarette smoke (e.g. smoothness and flavour). It should be noted that, even if manufacturers add sugars with the goal of "replacing" sugars lost during tobacco processing, the goal is to increase the palatability and the appeal of the product. Further, certain cigarettes may contain high levels of total sugars even if manufacturers do not add any sugar. These include cigarettes made with flue-cured or air-cured tobaccos, which are prevalent in Europe and other regions of the world. Some manufacturers may also use high-sugar tobaccos in cigarettes that are marketed as additive-free. For example, American Spirit cigarettes, which are marketed in the USA as containing only "tobacco and water", have a low concentration of sucrose (probably from the tobacco) but higher concentrations of fructose and glucose than other popular brands (Fig. 4.3A).

Fig. 4.3. Levels of soluble sugars in popular US cigarette brands: (A) Relative levels of fructose, glucose and sucrose and their sum in all the brands; (B) correlation between sucrose and the sum of glucose and fructose



Source: Stepanov et al., manuscript in progress

1 Stepanov et al., manuscript in progress

Cigars and cigarillos. Cigars usually contain relatively low levels of sugars, because most are made with air-cured and fermented tobacco and often do not contain added sugars *(23)*. Cigarillos (small, narrow cigars resembling cigarettes) may also contain relatively low levels of sugars; however, the sugar content of some is more similar to that of cigarettes *(5)*.

Addition of various high-intensity sweeteners to cigarillos has also been reported. Most of the surveyed top-selling US brands contained such sweeteners as glycyrrhizin (a sweet compound derived from the roots of the liquorice plant), acesulfame-K and sucralose *(22)*.

Pipe tobacco. No recent reports were found on sugars in pipe tobacco; however, previously published data indicate that the levels are likely to be similar to those in cigarettes *(3,11)*.

Waterpipe tobacco. Waterpipe tobacco contains the highest levels of sugars of all tobacco and nicotine products, with the weight of sugars exceeding the weight of tobacco in the same product by up to 64% (Fig. 4.2) *(25,27)*. Unlike cigarettes, most waterpipe tobacco contains fructose and glucose-based sugar additives (Table 4.2).

4.3.4.2 Smokeless tobacco

Studies of the levels of sugars in smokeless tobacco products indicate significant differences among product types, with high levels usually found in some chewing tobacco products (Table 4.2) *(3,20,23)*. While other smokeless tobacco products, such as moist snuff and snus, usually contain lower levels of sugars (Table 4.2), high-intensity sweeteners such as saccharine, sucralose and aspartame were reported in such products *(6)*.

Although smokeless tobacco products sold in India and other South Asian countries often contain molasses and other sweet ingredients, no data were available on the sugar levels in such products.

4.3.4.3 E-cigarettes and heated tobacco products

Limited data suggest that the concentrations of soluble sugars in e-cigarette liquids are lower than in smoked products (Table 4.2). As in cigarettes, however, the sucrose levels tend to be the higher and more variable than those of fructose or glucose. For example, Fagan et al. *(26)* (Table 4.2), who analysed 66 e-cigarette liquids, found sucrose at levels of 9.3–620 µg/mL and higher levels in flavoured varieties.

Sugar alcohols and synthetic sweeteners are also used in e-cigarette liquids. For example, sorbitol and ethyl maltol were found in some e-liquids at levels of < 0.003–0.089% w/w *(6)*. In a recent study in Austria, sucralose was detected in 43% of the commercially available e-liquids screened, at concentrations of 0.1 to > 0.5% *(28)*.

No published data were found on the levels of sugars and sweeteners in heated tobacco products.

4.3.4.4 Nicotine pouches

Limited data indicate that nicotine pouches frequently contain high-intensity sweeteners, such as acesulfame-K and sucralose, and that the levels of these sweeteners tend to be higher in varieties with a higher nicotine content (perhaps to mask the bitter taste of nicotine) *(7,29)*. The reported levels of acesulfame-K were 0.32–0.94 mg per pouch, and those of sucralose were 0.64–1.2 mg per pouch *(7)*.

4.4 Chemistry of the thermal degradation of sugars and sweeteners

Thermal degradation of sugars and sweeteners, which occurs during use of smoked and heated products such as cigarettes, waterpipes, e-cigarettes and heated tobacco products, generates a wide range of chemical compounds. Some of the compounds contribute to the aroma and smoothness of the smoke, and some are well-known toxicants and carcinogens.

The types and the levels of chemical compounds formed upon thermal degradation of sugars and sweeteners depend on the temperature at which the product is used. For example, while the temperatures in a burning cigarette are approximately 300–900 °C (depending on the distance from the burning tip), products such as waterpipes, e-cigarettes and heated tobacco products are used at much lower temperature ranges, reaching a maximum of 300–450 °C *(30–33)*. Therefore, the chemical composition of sugar-related emissions can vary considerably among such products.

Degradation of soluble sugars. Among the predominant products of the pyrolytic degradation of fructose, glucose and sucrose are furans (e.g. furfural and 5-hydroxymethylfurfural), pyrazines, pyridines, aldehydes and other carbonyls (e.g. formaldehyde, acetaldehyde, acrolein, diacetyl), polycyclic aromatic hydrocarbons (PAH), other volatile organic compounds (e.g. benzene, acrylamide) and organic acids (e.g. formic and acetic acid) *(15,16)*. The relative amounts of these compounds depend on the temperature, furans being more prevalent at lower temperatures and the prevalence of compounds such as aldehydes and PAH increasing at higher temperatures *(15)*. Some of these chemicals are also formed as the result of the reaction of sugar with other constituents in the emissions, such as via Maillard reactions *(15,34)*.

Degradation of sweeteners. Sugar alcohols and other natural and synthetic sweeteners that are found in e-cigarette liquids and some smoked products can also produce various toxic chemical compounds. For example, at the high temperatures relevant to smoked product combustion (e.g. > 500 °C), pyrolysis of the liquorice-derived glycyrrhizin yields 2,5-dimethylfuran, 2(3H)-furanone and xylene, among other compounds, and pyrolysis of sorbitol produces hydroxyacetaldehyde, hydroxyacetone, furfural, 1-(2-furanyl)-ethanone, benzene and phenol *(35,36)*. In products used at lower temperatures, heating of sucralose at 100–400 °C can produce polychlorinated aromatic hydrocarbons and polychlorinated dioxins and

furans *(37–39)*. Such reactions are catalysed by certain metals (e.g. aluminium, copper) and metal oxides, which are commonly present in the tobacco filler of smoked products and in some e-cigarette liquids (leaching from heating coils). In the presence of glycerol (commonly present in e-cigarettes and heated tobacco products), sucralose can form the carcinogenic 3-monochloropropanediol and several other chloropropanols *(40,41)*.

The impact of acids (e.g. pH-altering chemicals) and aromatic compounds on the attractiveness and implications for addictiveness are discussed in section 4. Product-specific contributions of sugars and sweeteners to the chemical profile of product emissions, with a focus on toxic constituents, are discussed in section 4.6.

4.5 Contribution of sugars to the abuse liability of tobacco and nicotine products

Sugars and sweeteners in tobacco and nicotine products contribute – directly or indirectly through the chemical constituents formed from their thermal degradation – to the attractiveness (palatability, appeal) and addictiveness of the products. These product characteristics define their abuse liability (i.e. the likelihood of developing biological and/or psychological dependence on a product) *(42–44)*. The mechanisms by which sugars contribute to these effects in various tobacco and nicotine products are outlined below and were discussed in the seventh report *(17)*.

4.5.1 Contribution of sugars to the attractiveness of tobacco and nicotine products

Cigarettes. Sugars and sweeteners are added to tobacco and nicotine products to reduce their harshness and bitterness and to enhance their taste and flavour characteristics. In smoked products, these effects are driven by chemical transformation of sugars during the burning of tobacco. For example, cigarette smoke contains significant amounts of alkaline constituents such as nicotine, other tobacco alkaloids and ammonia, which, in the absence of sugars, would make the smoke harsh and difficult to inhale *(15,45)*. Indeed, an industry study reported that acceptance of cigarette smoke by a panel of smokers was proportional to the sugar level in the tobacco *(2)*. The naturally present and added sugars increase the palatability of smoke by producing acetic and formic acids during tobacco combustion, which reduce smoke pH and thus decrease its harshness *(11)*. In addition, sugar caramelization and Maillard reactions that occur during tobacco burning produce aromatic compounds with woody, caramel, cocoa and other pleasant flavour notes, contributing to the taste and smell of the tobacco smoke *(15,18,46–48)*.

Waterpipes. The most popular varieties of waterpipe tobacco worldwide are the flavoured, highly sweetened ones, known as *moassel* or *maassel* (which

means "sweetened with honey") *(27,49–53)*. In studies of waterpipe tobacco users, most participants reported that the smoothness and the appealing taste and aroma of the waterpipe smoke were the main reasons for using sweetened waterpipe tobacco varieties *(54–56)*.

E-cigarettes and heated tobacco. Sugars and sweeteners in e-cigarette liquids and in heated tobacco products, if present, may contribute to the palatability of aerosols through many mechanisms, depending on the type of sugar or sweetener and on the temperature at which the device operates. First, a certain proportion of dehydrated sugars and sweeteners is likely to be transferred from e-cigarette liquid to the aerosol, rendering it sweet, as e-cigarettes operate at relatively low temperatures that do not result in complete sugar pyrolysis. This may also be true for heated tobacco products, although the temperatures at which they operate are higher. Secondly, as some thermal degradation is likely to occur, sugars may contribute to the aerosol flavour by adding certain aromatic products of degradation. Thirdly, as evidence of pyrolysis has been reported for heated tobacco products *(57)*, sugars (if present) may contribute to the smoothness of the product aerosol by altering its pH. These expectations are based on the chemistry of thermal degradation of sugars and their effect on the palatability of cigarette smoke. Research on the impact of sugars and sweeteners on the attractiveness of e-cigarettes and heated tobacco products is, however, lacking.

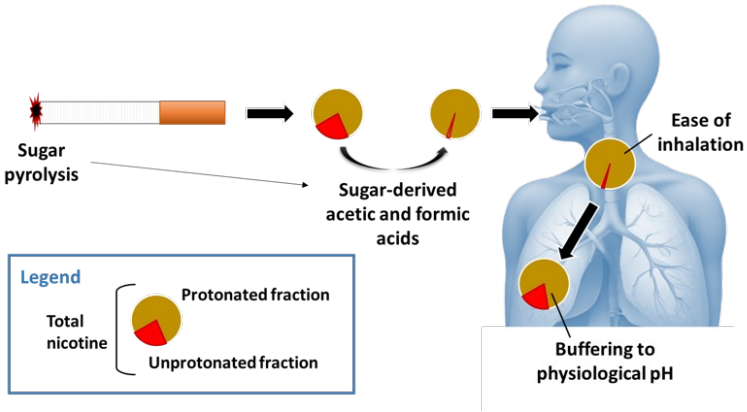
Smokeless tobacco and nicotine products. There is no thermal degradation in use of smokeless tobacco and nicotine pouches. Sugars and sweeteners serve as flavourants in their original forms, adding a sweet taste and appealing flavours.

4.5.2 Contribution of sugars to the addictiveness of tobacco and nicotine products

4.5.2.1 Effects on the bioavailability of nicotine in product emissions

By altering the pH of product emissions, sugars are likely to contribute to the addictiveness of cigarettes and other smoked products (Fig. 4.4). While the actual mechanism by which sugars increase the smoothness of smoke is based on a reduction of free-base (i.e. biologically available) nicotine, which is known for its harshness, the smoother smoke still contains the same amount of total nicotine. Therefore, at similar levels of nicotine in tobacco filler, products with higher levels of sugars facilitate deeper inhalation of the smoke and, as a consequence, smoking delivers larger amounts of total nicotine deeper into the lung than from those with lower levels of sugars *(11)*. The pH-buffering capacity of the lung epithelium increases the bioavailability of nicotine. Approximately 19% of total nicotine is present in the biologically available free-base form at the physiological pH of 7.4, while 1–2% of total nicotine is present at the typical pH of cigarette smoke *(34,58)*. Thus, sugars might indirectly contribute to product addictiveness by increasing nicotine delivery to the lungs and the bloodstream of users.

Fig. 4.4. Impact of sugars on nicotine delivery



4.5.2.2 Contribution to the addictive properties of nicotine

Smoked products. Another mechanism by which sugars can contribute to product addictiveness is by adding to the reinforcing effects of nicotine. For example, acetaldehyde, one of the major products of the thermal degradation of sugars, has been shown to increase dopaminergic neuronal activity and enhance nicotine self-administration in laboratory animals *(12,13)*. Acetaldehyde and formaldehyde (another product of sugar decomposition) are also precursors of the beta-carbolines harman and norharman, which inhibit monoamine oxidase and increase nicotine self-administration in rats *(14)*. While some studies reported an association between plasma harman and norharman in smokers and the number of cigarettes smoked, no well-designed studies with human participants are available on how sugars in smoked tobacco products contribute to the addictive effects of nicotine and affect use.

Smokeless tobacco and nicotine products. Sugars and sweeteners in non-smoked products give such products a sweet taste and appealing flavour, which may mask the bitterness of nicotine and stimulate saliva, allowing more frequent and intense product use, thus indirectly contributing to development of nicotine addiction. A recent study in laboratory animals of nicotine pouches provides support for this expectation, showing that, at the levels present in the pouches, artificial sweeteners increase nicotine self-administration and decrease aversion to higher nicotine concentrations *(7)*. There have been no reports, however, of research on the effects of sugars and sweeteners on the addictiveness of smokeless tobacco products.

4.6 Implications of sugars and sweeteners for the toxicity of tobacco and nicotine products

4.6.1 Contribution of sugars and sweeteners to toxic emissions from various tobacco and nicotine products

4.6.1.1 Contribution of sugars to cigarette smoke emissions

Sugars are almost completely degraded when cigarettes are burnt, only approximately 0.5% of their content in tobacco being transferred intact into the smoke *(15,34,59)*. Studies in which sugars were added to experimental cigarettes have shown that such addition results in quantifiable increases in the concentrations of several harmful carbonyls (e.g. formaldehyde, acetaldehyde, acetone, acrolein, crotonaldehyde, propionaldehyde) and of furfural and other furans *(15,60)*.

While studies with experimental cigarettes are informative, assessment of the association between sugar levels in the tobacco filler of commercial cigarettes and the relevant toxicant emissions in the smoke provide better understanding of the real-world implications for users. In a study of 50 brands of commercial Dutch cigarettes, published after the previous WHO TobReg report on sugars, higher levels of sugars and humectants in tobacco filler were associated with higher levels of formaldehyde, acetaldehyde, acrolein and 2,5-dimethylfuran in mainstream cigarette smoke *(21)*. In that study, the relative contributions of sugar-derived formaldehyde, acetaldehyde and acrolein to the total smoke emissions of these constituents were estimated to be 85%, 6% and 17%, respectively. In a recently completed study of 52 popular US cigarette brands, the association between sugar levels in tobacco filler and levels of toxicants in cigarette smoke, expressed per mg nicotine, were assessed to account for the effect of filter ventilation and other product characteristics.[2] Multivariate analysis with adjustment for cigarette length and menthol status showed that higher levels of sucrose in tobacco (but not glucose or fructose) were statistically significantly associated with higher smoke yields of formaldehyde, acetaldehyde, acetone, acrolein, propionaldehyde, crotonaldehyde, butanone and butyraldehyde. These findings indicate that people who smoke cigarettes with higher added sugar content, independent of other product characteristics, are exposed to higher levels of these and potentially other toxicants and carcinogens with each inhaled dose of nicotine.

4.6.1.2 Contribution of sugars and sweeteners to waterpipe tobacco smoke emissions

Heating of waterpipe tobacco results in the transfer of sugar decomposition products, particularly furans, to the waterpipe smoke *(61–63)*. Because of the lower temperatures of waterpipe tobacco smoke than those in cigarette smoke, a significant fraction of dehydrated sugars and glycerol from waterpipe tobacco

2 Hansen et al., manuscript in preparation

is transferred to the smoke unchanged, resulting in lower levels of certain low-molecular-weight carbonyls than would be formed in the smoke of conventional cigarettes *(63)*. In addition, waterpipe smoke is diluted by the water in the bowl, potentially diluting the products of sugar decomposition *(62)*. Nevertheless, for every gram of tobacco smoked, waterpipe tobacco users inhale roughly the same amount of formaldehyde, six times more furfural, three times more furfuryl alcohol and 250 times more 5-hydroxymethylfurfural than cigarette smokers *(31)*. Furthermore, at least 4 g of waterpipe tobacco are used in a single session, which is much more than the amount of tobacco contained in a single cigarette *(62)*.

4.6.1.3 Contribution of sugars and sweeteners to e-cigarette emissions

Few studies have been conducted on the impact of soluble sugars in e-liquids on e-cigarette emissions. Experiments with laboratory-made e-liquids showed that sucrose and glucose in e-liquids could degrade during e-cigarette use to form 5-hydroxymethylfurfural and furfural *(64)*. As high-intensity sweeteners are found in many e-liquids, studies of their impact on e-cigarette emissions are important. These have shown that, during e-cigarette use, degradation of sucralose produces hydrochloric acid, which participates in reactions with propylene glycol and glycerol to form chloropropanols, other chlorinated compounds, aldehydes and hemiacetals *(65–67)*. Studies should be conducted to better characterize the contribution of sugars and sweeteners to the toxicity of e-cigarette aerosols.

4.6.1.4 Contribution of sugars and sweeteners to heated tobacco product emissions

No studies of the potential association of sugars in heated tobacco products with product emissions were available at the time of this report. Levels of furans, which can be formed as a result of sugar pyrolysis, were reported to be higher in heated tobacco product aerosols than in cigarette smoke *(68)*. Chloropropanols, which can be formed from sucralose, were also reported to be present in a heated tobacco product aerosol *(69)*. Research should be conducted to determine the types and levels of sugars and sweeteners in heated tobacco products, including in the recently introduced flavour capsules in the mouthpiece of heated tobacco sticks *(70)*, and their potential impact on the toxicant profile of aerosols.

4.6.2 Implications of toxicity for people who smoke or use heated tobacco and nicotine products

Given the complexity of the emissions from smoked tobacco and nicotine products, studies of the association between sugars in these products and the levels of harmful exposures and health effects in laboratory settings (e.g. in vitro, in vivo) or in people who use these products are difficult to design and are therefore lacking. While there is insufficient direct evidence of a measurable impact on toxic

outcomes of emissions, many compounds resulting from sugar decomposition are toxicants and carcinogens, with a well-established role in the pathogenesis of various diseases in humans. Therefore, sugars in tobacco and nicotine products are likely to contribute to harmful exposures and to be responsible for the negative health outcomes associated with use of these products.

Carcinogenic effects of sugar-associated constituents. Many products of sugar degradation have carcinogenic properties. For example, furans are hepatic toxicants and carcinogens and can potentially contribute to renal carcinogenicity *(71)*; formaldehyde and acetaldehyde cause respiratory tumours in laboratory animals *(72,73)*; and acrolein is considered to be a pulmonary carcinogen *(74,75)*. Crotonaldehyde and acrylamide can form DNA adducts in the human lung, and acrylamide is genotoxic and carcinogenic in many organs *(76,77)*. Benzene, which is classified as a human carcinogen, causes leukaemia and is associated with multiple myeloma and non-Hodgkin lymphoma *(73)*. Many PAHs are also potent carcinogens and are widely considered to be major contributors to lung cancer in smokers *(78,79)*.

Cardiopulmonary toxicity of sugar-associated constituents. Most such constituents are also inflammatory agents and respiratory and cardiovascular toxicants. For example, acrolein causes inflammation, is an intense pulmonary irritant and toxicant and induces dose-dependent cardiovascular toxicity *(74,80–82)*. In a risk assessment study, it was proposed that acrolein is one of the main cigarette smoke constituents responsible for cardiopulmonary diseases resulting from smoking *(83)*. Exposure to PAH is strongly implicated in cardiovascular disease and death *(84)*. A study of controlled exposure to acetic acid increased self-reported ratings of nasal irritation in healthy adults and nasal obstructive responses among individuals with allergic rhinitis *(85,86)*.

4.6.3 Implications of toxicity for people who use smokeless tobacco and nicotine products

High levels of sugars in smokeless tobacco may contribute to toxicity in users by several potential mechanisms. First, the high sugar content in some smokeless tobacco products may contribute to the high prevalence of dental caries, periodontal disease and other non-carcinogenic oral and dental health outcomes in users *(87)*. For example, use of smokeless tobacco has been clearly associated with such adverse outcomes in India *(88)*. In the USA, assessment of dental health status in the National Health and Nutrition Examination Survey showed that, consistent with the corresponding differences in sugar content (Table 4.2), users of chewing tobacco had higher numbers of decayed teeth than users of moist snuff, with a dose–response relation between the number of packages of chewing tobacco used per week and the odds of root-surface caries *(89)*. In addition, the metabolism of sugars by oral bacteria can lead to production of DNA-damaging

acetaldehyde, which could contribute to the risk for oral cancer in users *(90,91)*. Furthermore, concern has been raised that swallowing rather than expectorating saliva during use of a product with a high sugar level could contribute to increasing the level of glucose in blood *(92)*. Research on the potential impact of sugars and sweeteners in smokeless tobacco and nicotine products on these health outcomes is, however, limited.

4.7 Effects of sugars on perception and use of tobacco and nicotine products

The few studies of consumer awareness of sugars and their effects in tobacco and nicotine products indicate that the level of awareness is generally low. For example, in a study of awareness of sugars in cigarettes, less than 6% of participants reported that they knew that sugars are added to cigarettes *(93)*. Once they were informed about sugars in tobacco products, however, people who smoked considered that added sugars in products increase the consumption and addictiveness of products, suppress bitter taste perceptions and mask the odour of secondhand smoke *(94,95)*. Study participants were generally unaware of the potential contribution of sugars to product toxicity and health risks *(93–95)*. In one study *(93)*, some participants stated that learning more about potential sugar-associated toxicity could impact their product use patterns and quit attempts. These limited findings suggest that informing users about sugars in tobacco and nicotine products could contribute to reducing the prevalence of use.

Despite low awareness about sugars in tobacco products among consumers, the impact of sugars on product perceptions and use patterns is likely to be profound. The evidence available for other product characteristics that affect product palatability indicates that it is plausible that sugars in tobacco and nicotine products contribute to misperceptions of product safety, to higher intensity of product use and potentially to product initiation by novice users.

Misperceptions of risk. Users of tobacco and nicotine products that are smooth and flavourful tend to consider such products safer than other products on the market. For example, people who smoke cigarettes with ventilated filters (small holes in cigarette filter tips that dilute the smoke with air) reported that their cigarettes tasted "lighter" and "smoother" than regular cigarettes and considered that their exposure to harmful smoke constituents was reduced *(9,96–98)*. Even removal of descriptors such as "light" and "ultra-light" from cigarette packs did not affect such beliefs *(99,100)*. Similar misperceptions of risk are observed with the perceived smoothness of mentholated cigarettes *(101–103)* and are likely to apply to products that taste sweeter because of the addition of sugars or sweeteners.

Studies have also shown that flavoured waterpipe tobacco, which contains the highest levels of sugars of all tobacco and nicotine products, is misperceived by users as less harmful than other forms of tobacco *(104)*. There has been explicit

marketing of some sweet-flavoured waterpipe tobacco brands as healthy, natural alternatives to cigarettes *(63,105,106)*. Such misperceptions and marketing practices can contribute to continued product use.

Increased intensity of product use. Users of tobacco and nicotine products that are perceived as less harsh tend to use them at a higher intensity, because they are easier to inhale and/or in an attempt to achieve a satisfying intake of nicotine. Ventilated cigarettes can be used again as an example. The "lightness" (e.g. reduced harshness) of the smoke of ventilated cigarettes, which is associated with the perceived lower nicotine intake, results in more intense smoking behaviour, such as blocking filter vents, drawing larger puffs and inhaling more deeply *(107,108)*. Another relevant example is the introduction of nicotine salts into e-cigarette devices such as JUUL, which minimized the harshness of the e-cigarette aerosols and facilitated intake of much higher nicotine levels than from the harsher versions of e-cigarettes *(109)*. More intense product use is not only associated with a higher level of addiction and sustained use *(110,111)* but also exposes users to higher doses of the toxicants and carcinogens present in the product.

Potential role in initiation. Products with masked harshness and pleasant flavours appeal to youth and non-users. For example, it has been shown that menthol cigarettes are disproportionately used by youth and young adults, probably due to taste preferences, sensory properties and easier inhalation *(112)*. Flavoured, sweetened waterpipe tobacco was reported by new users to be enticing *(103)*. Sugar- and sweetener-associated flavours such as caramel, liquorice and cocoa are also appealing to youth, and therefore their presence in tobacco and nicotine products may promote initiation and progression from occasional to regular product use *(113–115)*.

4.8 Tobacco industry research on sugars in tobacco products

As toxicological studies are resource- and time-consuming, public health researchers and regulators, of necessity, in the absence of alternative source of information, sometimes have to rely on research and the conclusions of the tobacco industry in evaluating the state of science on a particular product design feature. Such research, however, is conducted for the purpose of advancing the industry's commercial interests and may not be designed to obtain adequate, unbiased data and/or may be interpreted and communicated by the industry in a misleading way. In 1994, about 4000 confidential internal documents were leaked from the Brown & Williams Tobacco Corporation, providing the public with evidence, for the first time, that the tobacco industry was not only aware of nicotine's addictive potential but also carefully monitored and manipulated the nicotine levels in their products. Furthermore, the documents revealed that the industry was not ignorant of the adverse health effects of cigarettes *(116–118)*. That same year, the attorneys general of the US states of Minnesota, Mississippi, Texas and Florida filed separate lawsuits

against the tobacco industry, and the other 46 states shortly followed suit. By 1998, the industry had signed the Master Settlement Agreement, which resulted in the release and public availability of some 70 million pages of previously confidential industry documents *(116)*. Review of these documents, which are now part of the Truth Tobacco Industry Documents collection, housed online by the University of California at San Francisco, can provide insights into the industry's approach to research on the effects of sugars in tobacco products.

4.8.1 Industry approach to testing the toxicity of ingredients

At least as early as the 1990s, tobacco companies, including R.J. Reynolds and Philip Morris, adopted so-called "tiered strategies" for toxicity testing of tobacco ingredients, which largely mirror the tiered approach recommended by the US FDA to toxicological testing of additives used in food *(119)*. For example, in R.J. Reynolds' tiered strategy, a decision tree was used to determine the degree of concern about an ingredient according to exposure, the level of the ingredient in the product, information available on the ingredient and the ingredient's role in the product or manufacturing process *(120)*. Likewise, Philip Morris determined its level of concern and subsequent toxicology testing strategy for an ingredient according to its potential to contribute to the biological activity of cigarette smoke *(121)*.

With these approaches, sugars should be considered to be at the highest level of concern, because most cigarette tobacco in commercial products contains high levels of sugars by weight. As sugars are ingredients of high concern, the tiered strategies would require evaluations of changes in smoke chemistry, complemented by assessments of genotoxicity, including assays for bacterial reverse mutation (Ames assays) and sister chromatid exchanges, assessments of cytotoxicity, including neutral red uptake assays and in vivo assays, including 90-day or 13-week nose-only smoke inhalation studies in rodents.

4.8.2 Findings of industry research on toxicity

Industry and/or industry-sponsored research on the contribution of individual sugars to the toxicity of cigarette smoke in vitro or in vivo according to their proposed tiered approaches is limited. In some of the major studies on the role of sugars in toxicity, additional ingredients in the test cigarettes were manipulated simultaneously. For example a report by Philip Morris entitled "Evaluation of Sucrose for Use as a Cigarette Ingredient" was based on data from experiments that were designed to test 333 ingredients. In that report, Philip Morris described one study in which study cigarettes with sucrose contents of 3.3% and 4.6% were tested; however, it noted that those cigarettes contained 10.79% and 14.79% additives by weight overall, so that differences in findings for the test cigarettes used in this study are not solely attributable to the sugars *(122)*. Similarly, many reports on toxicity testing of sugars and sweetening agents from the Lorillard Tobacco

Company involved test cigarettes with different combinations of sugars and sweeteners at various concentrations *(123)*, making it difficult to draw conclusions on their contributions to smoke toxicity. Because of the complexity of evaluating such studies, the overview of industry toxicology testing summarized below is limited to a few representative studies in which only one sugar or sweetener at a time was manipulated.

Smoke chemistry and pyrolysis studies. Philip Morris contracted the IIT Research Institute (IITRI) to analyse the chemistry of mainstream smoke from cigarettes containing target levels of up to 10% (100 000 ppm) inverted sugar or sucrose. The final IITRI reports showed statistically significant increases in aldehyde yields per mg tar, specifically formaldehyde, acetaldehyde, propionaldehyde and acrolein, between the 0% (0 ppm) and 10% (100 000 ppm) invert sugar cigarettes; the increases were explicitly attributed to the combustion of the added invert sugar *(124)*. For the sucrose-enriched cigarettes, the results were inconsistent, with both increases and decreases in aldehyde levels reported among the range of levels of added sucrose *(124)*. Published reviews by the tobacco industry were similarly inconsistent. For example, some reviews reported that adding sugars to cigarette tobacco increased phenol, furans, organic acids, furfural and formaldehyde, but did not acknowledge acetaldehyde or acrolein emissions *(34,125)*, even though an industry study dating back to 1971 reported that acetaldehyde was a major product of sugar decomposition in tobacco *(59)*.

In vitro genotoxicity and cytotoxicity studies. IITRI also assessed the genotoxicity and cytotoxicity of test cigarettes with added invert sugar or sucrose and reported no statistically significant difference in mutagenicity or cytotoxicity, measured by the Ames or neutral red uptake assay, respectively, between the test cigarettes containing 0% (0) ppm and any level of added sucrose or invert sugar up to concentrations of 10% (100 000 ppm) *(126–129)*. Similarly, a study by R.J. Reynolds found no difference between smoke condensates from cigarettes prepared with low or high levels of high fructose corn syrup in a neutral red uptake assay in Chinese hamster ovary cells *(130)*.

90-day smoke inhalation studies. In the late 1990s, Lorillard Tobacco Company contracted IITRI to conduct 90-day nose-only smoke inhalation studies in rats exposed for 13 weeks to smoke from unspecified test cigarettes containing either 1x or 2x levels of sugar A, sugar B or both sugars, with air-only (sham) and a reference cigarette (no sugar added) as control conditions. Neither the exact concentration nor the identity of the sugars was specified in the report. Decreased body weights, increased carboxyhaemoglobin and significant adverse differences in haematological parameters were detected in the test groups relative to the sham group; however, the report stated that these findings were sporadic and unrelated to the sugar exposure. Respiratory tract lesions were seen in all smoke-exposed groups, but the effect did not differ according to sugar level or type. Liver and spleen weights were significantly increased over that in the reference group in

2x A male rats. The report concluded that adding various amounts and types of sugars to cigarette tobacco does not significantly affect the outcomes of whole-smoke exposure in rats *(131)*.

4.8.3 Limitations of industry research on toxicity

The studies and findings described above are a representative sample of the studies conducted on individual sugars as cigarette ingredients and their conclusions. The conclusions reported in the industry studies sometimes contradict industry-independent findings on the impact of added sugars on toxic cigarette emissions, raising concern about reliance on industry data when independent research is not available. No toxicological (in vitro or in vivo) studies conducted after the early 2000s on cigarette tobacco are available in the document archive, and there is little evidence of any tobacco industry studies on potential toxicity due to added sugars in other tobacco products. While standard toxicity assessments were used in the studies conducted by the industry, no assessments of the toxicity of sugars as tobacco product additives have been conducted with more advanced, sensitive methods to identify effects at cellular or molecular level. Furthermore, many of the tests used in the industry studies are of limited relevance to known mechanisms of cigarette smoke toxicity in humans, as most of the tests were conducted in bacteria or non-human mammalian cells, such as Chinese hamster ovary cells. While the latter are relatively standard approaches for mutagenicity testing and can be of value, they do not appear adequate for the complex profile of sugar decomposition chemistry and the overall complexity of emissions. Therefore, additional data are required. Sub-chronic studies of rodent smoke inhalation (90-day exposure) may be the most predictive of outcomes in people who smoke, but the duration of those studies was too short for proper assessment of endpoints indicative of carcinogenicity. It is well known that, while rodent inhalation studies can be useful for assessing lung cancer risks due to environmental exposures, differences in the pathobiology of human and rodent lung cancers can make it difficult to translate rodent outcomes to assessment of human risk *(132)*. No tobacco industry data are available on assessment of biomarkers from people who smoke to examine potential differences in exposure or biological effects attributable to smoking cigarettes with high levels of sugars.

4.8.4 Exploration or use of alternatives to sugars by the industry

Examination of tobacco industry documents indicates that at least some tobacco companies are aware of the concerns associated with sugars as ingredients and have been exploring alternatives to sugars that will retain the desirable properties of products. For example, a document from Lorillard in 2001 describes a project called "Diminished harm tobacco products (DHTP) B-1001: carbonyl compounds", in which the authors acknowledge that the major source of carbonyl compounds

in tobacco smoke is sugars, among other precursors *(133)*. The purpose of B-1001 was thus to minimize undesirable carbonyl compound formation in smoke while retaining carbonyls with desirable properties. To do this, a "Carbonyl Task Group" assembled by Lorillard proposed interventions such as partially replacing high sugar tobacco types in cigarette tobacco blends and exploring application of a mixture of desirable carbonyl compounds to a tobacco blend to retain the aromas typically imparted by sugars without the precursor sugars *(133)*. Another example is a memorandum dated 1954 that suggests that sugars in chewing tobacco be replaced by saccharin or other high-intensity sweeteners to retain the sweetness of the product while avoiding the formation of off-flavours that were attributed to oxidation of sugars over time *(134)*.

4.9 Regulation of sugars

As summarized above, there is a substantial body of evidence that sugars and sweeteners are being used by manufacturers to enhance the palatability of tobacco and nicotine products, which poses increased risks of addiction and toxicity to users. In the WHO FCTC guidelines, WHO advises Member States to adopt comprehensive tobacco control measures *(1)*, which may include sugar regulation, reporting to regulators and disclosure to the public. Some countries have either implemented or proposed such regulation of sugars in tobacco and nicotine products, mainly under the umbrella of additives.

4.9.1 Examples of relevant regulation of tobacco and nicotine products

Most bans on additives, which target mainly characterizing flavours but may also include sugars and other palatability-relevant additives, are based on evidence that such additives can facilitate tobacco use initiation and continuation because they make tobacco products more attractive and palatable (particularly to adolescents).

The European Tobacco Product Directive. A ban on characterizing flavours in cigarettes and roll-your-own products was imposed in the European Union (EU) in 2014 in Directive 2014/40/EU (135). In addition, product manufacturers are required to disclose (annually) the composition of all marketed tobacco products, including the amounts and types of added sugars, tobacco variety or blend, curing method and other characteristics. One challenge in assuring manufacturers' compliance with the Directive is that it allows manufacturers to add back the amounts of sugars lost during tobacco processing, without providing specific guidance on how the initial sugar content should be determined and recorded. Another limitation is the definition of "characterizing flavours", which is somewhat subjective and may not include subtle flavourings that are not clearly distinguishable.

Health Canada. Sugars and many other additives in cigarettes, little cigars, cigarillos and blunt wraps were banned by Health Canada in 2009 (amendment

to the Tobacco Act, Bill C-32) *(136)*. Introduction of the ban was associated with a decrease in the use of cigarillos among Canadian youth *(137)*. Manufacturers and importers are also required to provide information on all tobacco product ingredients.

US FDA. Under the authority granted in 2009 by the US Family Smoking Prevention and Tobacco Control Act, the US FDA banned cigarettes containing certain characterizing flavours *(138)*. No regulations have been enacted, however, for the sugar content of cigarettes or other tobacco and nicotine products.

Brazilian Health Regulatory Agency. In 2012, a resolution was adopted prohibiting some additives in tobacco products, including sweeteners, honey, molasses, fruit extracts and substances that can impart a sweet flavour (RDC 14/2012) *(139)*. As in the EU Directive, an exception was made for sugar, so that manufacturers are allowed to replace the quantity lost during tobacco processing. Implementation of this resolution has, however, stalled since September 2013, because of a lawsuit filed by the National Confederation of Industries on behalf of tobacco product manufacturers.

Research on the use of tobacco and nicotine products before and after introduction of a ban on flavours in some countries provides evidence of the beneficial impact of such bans. For example, increased rates of quitting and of menthol cigarette use have been reported in Netherlands (Kingdom of the) *(140)*, Canada *(141)* and the United Kingdom *(142)*. Research in the USA, however, suggests that banning flavours in some but not all tobacco and nicotine products (e.g. in e-cigarettes but not in smoked products) may lead to a shift to use of products with flavoured options *(143,144)*. Therefore, to be effective, a ban on flavours should cover all tobacco and nicotine products.

4.9.2 Challenges associated with regulating sugars in tobacco and nicotine products

Several actual and potential challenges should be taken into account when considering regulation of sugars and sweeteners in tobacco and nicotine products. Some of the challenges are specific to sugars and sweeteners, while others are common to any effort to regulate these products.

Industry claims that sugars lost during tobacco processing must be added back, in unspecified amounts. The reason for replacing sugars is, however, to reduce the bitterness and harshness of tobacco and cigarette smoke. Claims that the addictive and deadly product, which is a major cause of disease and death globally, should be made more palatable are specious.

Industry lobbying to prevent implementation of regulatory decisions. In addition to the experience in Brazil, examples include challenges to implementing the proposed product standards in New Zealand (nicotine reduction) and the USA (nicotine reduction and menthol ban).

Industry history of circumventing bans:

- Use of synthetic substitutes that may not be defined as sugars or sweeteners: For example, in response to imposed and/or expected bans on the use of menthol in tobacco and nicotine products in the USA, manufacturers began using non-menthol synthetic cooling agents in various products, including cigarettes, e-liquids and nicotine pouches *(145–148)*. Use of synthetic nicotine and the synthetic nicotine analogue 6-methyl nicotine emerged after the US FDA extended its authority to include all products that contain tobacco-derived nicotine *(149–150)*. Such substitutes may raise concern about elevated toxicity and addictiveness.
- *Use of accessories such as filter capsules*. Various flavour accessories, such as flavour capsules, drops and sprays, were introduced following bans on flavoured tobacco and nicotine products, as they may not be covered by regulations on the base product *(151)*.
- *Shifting to tobaccos high in natural sugar content*. Cigarettes made with Virginia and other high-sugar tobaccos are already available on markets globally. If the majority of cigarettes are changed to contain such tobaccos, regulation of added sugars will have no meaningful impact. Further, as seen with American Spirit cigarettes in the USA, industry may engage in deceptive marketing, promoting such cigarettes in a way that implies reduced harm. Therefore, regulation of sugars in tobacco products might have to include a limit on the levels of natural sugars.
- *Manipulation of other product characteristics*. Manufacturers may resort to using other pH modifiers or to changing filter ventilation or other characteristics to maintain the desired product palatability in the face of regulations restricting the use of sugars and sweeteners. Such product modifications may affect appeal, addictiveness and/or toxicity to a similar or greater degree than sugars. Therefore, manufacturers should be required to report any such product modifications in response to a sugar ban.

4.10 Summary and conclusions

Sugars and sweeteners remain key components of most tobacco and nicotine products. The types and levels of sugars and sweeteners vary widely by product type. Data on levels are accumulating but remain limited. Newer products tend to contain high-intensity sweeteners, including synthetic sugar substitutes.

There is accumulating evidence of the contribution of sugars and sweeteners to the toxic emissions of smoked and heated products, including distinct chemical profiles resulting from decomposition of sugars at lower temperatures (in products

that are heated rather than smoked) and those of sugar substitutes and synthetic sweeteners. Direct evidence of the additive effect of sugars on health risks in users is, however, lacking.

There is no doubt that sugars and sweeteners contribute to the appeal of tobacco and nicotine products by improving their smoothness and flavour. In addition, sugars and sweeteners in tobacco and nicotine products are probably sustaining product use by contributing to misperceptions of risks, to higher intensity of product use and to initiation of product use.

While there is no thermal decomposition of sugars and sweeteners in smokeless tobacco and nicotine products, there is accumulating evidence of their potential contribution to product addictiveness as well as suggestive evidence that sugars in smokeless products may contribute to the risk of oral cancer.

The tobacco industry has invested a significant amount of research into understanding how to use sugars to make their products attractive and addictive. At the same time, their research into the potential contribution of sugars to product toxicity and carcinogenicity has been minimal.

Added sugars and sweeteners are regulated in some countries, usually as part of the overall effort to ban additives that contribute to product attractiveness. Most countries, however, face continuous industry efforts to undermine tobacco control. It is important to implement stricter regulation of sugars and to foresee and monitor any circumvention.

4.11 Areas for research and future directions

As summarized in the previous section, several key research areas are relevant to sugars and sweeteners in tobacco and nicotine products, the results of which could strengthen the evidence already available:

- current, country-specific data on the types, levels and variation of sugars and sweeteners in tobacco and nicotine products, including e-cigarettes, heated tobacco products and nicotine pouches;
- studies in humans and laboratory animals to characterize the impact of sugars and sweeteners on the addictiveness of tobacco and nicotine products, including patterns of product use and mechanistic research on potential augmentation of the addictiveness of a product beyond the effects from nicotine;
- quantitative data on the relative contribution of sugars and sweeteners to the yields of relevant constituents (e.g. aldehydes, furans, chloropropanol, hemiacetals) in emissions of products other than cigarettes, as well as emission pH and unprotonated nicotine level;
- studies (in vitro, in vivo, human) to quantify potential enhancement by sugars and sweeteners of the toxic effects of tobacco and nicotine

products, including measurement of biomarkers and the resulting disease incidence and prevalence; and

- studies of perceptions of sugars in tobacco and nicotine products, including potential misperceptions of reduced harm, and the communication strategies for addressing misperceptions.

4.12 Policy recommendations

Regulation of sugar and sweeteners in tobacco and nicotine products could result in simultaneous reductions in product attractiveness and addictiveness and the associated harm to users, as recommended in the Partial guidelines for implementation of Articles 9 and 10 of the WHO FCTC *(1)*. This can be achieved by banning added sugars and sweeteners, setting limits on the total sugar content in finished products and mandating relevant disclosures by manufacturers. The following specific policy recommendations are proposed, based on the conclusions of this review.

- Mandate disclosure of the amounts of all naturally present sugars and of added sugars and sweeteners in tobacco and nicotine products and, as applicable, in emissions. The amounts of each sugar or sweetener should be disclosed individually rather than the total content.
- In view of health concerns about the use of sugars and sweeteners in tobacco and nicotine products, which influence their attractiveness, addictiveness and toxicity, inform the public about their presence in these products and their effects.
- Disallow exceptions for replenishing sugars removed during the processing of tobacco, and extend this to any additives that might enable product manipulation by manufacturers to circumvent sugar bans (for example use of novel synthetic substitutes).
- Mandate manufacturer disclosure of product characteristics and of the harmful and potentially harmful contents and emissions of tobacco and nicotine products, independent of their known relation to sugars and sweeteners, with the standard operating procedures for the WHO Tobacco Laboratory Network analytical methods, as applicable.
- Support country-relevant research independent of the tobacco industry on the effects of sugars and sweeteners on tobacco and nicotine on product appeal, addictiveness and toxicity, with a particular focus on the upper limits of the total levels of sugars and sweeteners in finished products, including natural sugars, should a Member State consider such a regulatory measure.

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5. Cigarette filters: implications for smoking behaviour, health effects and the environment

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Contents

Abstract
5.1 Introduction
  5.1.1 Scope and aim
  5.1.2 Methods
5.2 History, marketing and types of filters
  5.2.1 Development and introduction of cigarette filters
  5.2.2 Marketing and consumption patterns of filtered cigarettes
  5.2.3 Types of cigarette filters
5.3 Effects of filters on smoke emissions, smoking intensity and health
  5.3.1 Effects of filter ventilation
  5.3.2 Effects of charcoal filters
  5.3.3 Health implications of filters
5.4 Perceptions of cigarette filters
  5.4.1 Misconceptions of the effectiveness of filters in reducing human harms
  5.4.2 Public knowledge about filters and attitudes towards regulatory policies
5.5 Environmental impacts of discarded cigarette filters
  5.5.1 Chemical toxicity of cigarette butt waste
  5.5.2 Plastic pollution from cigarette filters
  5.5.3 Biodegradability of filters
  5.5.4 Recycling schemes
  5.5.5 Human health implications of discarded cigarette butts
  5.5.6 Harm to ecosystems
5.6 Summary
5.7 Conclusions
5.8 Research gaps, priorities and questions
5.9 Regulatory options regarding cigarette filters
  5.9.1 Policy options
  5.9.2 The current regulatory environment
5.10 Main recommendations
References

Abstract

Cigarette filters have been used by the tobacco-industry as a marketing tool since the 1950s. They not only make cigarette smoking more palatable but also mislead consumers into thinking that their health risks are substantially reduced when they smoke filtered cigarettes. Although machine-smoking measurements of tar, nicotine, and carbon monoxide are lower in filtered than unfiltered cigarettes, the difference may not reflect the true exposure of people who smoke to toxicants. Filtered cigarettes have not prevented the continued epidemic of smoking-attributable diseases. In addition, the predominant cell type of lung cancer caused by smoking has changed from small-cell and squamous-cell to adenocarcinoma, potentially reflecting the near universal adoption of filters, the addition of filter ventilation, the manipulation of nicotine and other chemical content in tobacco and other changes in commercial cigarette design. Last but not least, people who smoke discard trillions of poorly degradable cellulose acetate filters globally each year, which are a source of microplastics and chemical hazards. Discarded filters retain some of the nicotine, metals and other toxicants from smoked filtered cigarettes that contaminate the environments into which they are discarded.

Despite the lack of evidence that filters substantially reduce health risks and the evidence that filters contaminate the environment, misperceptions about filters' function and composition persist. Regulation of both demand and supply of tobacco is required to reduce the attractiveness of filtered cigarettes and their adverse environmental impact. Interventions include information campaigns to remove public misconceptions about filters, banning the sale of filtered cigarettes, and assessing use of extended producer responsibility fees to recover the costs of environmental harm. Important post-implementation considerations for filter bans include providing a clear explanation to the public of the rationale of the ban, building public support and continued smoking cessation interventions with approved cessation tools of proven efficacy and safety. It will be also important to monitor cigarette manufacturers' compliance to ensure that the industry does not co-opt this policy measure for reputational and/or marketing gain.

Keywords: Cigarette filters, cellulose acetate, health effects, tobacco product waste, environment

5.1 Introduction

More than 90% of the 4.78 trillion commercial cigarettes sold in 2020 *(1)* were filtered *(2)*. While the incidence rates of small-cell and squamous-cell lung carcinoma have been decreasing since the 1970s due to the overall reduction in smoking prevalence, the incidence of lung adenocarcinoma has increased and is now the predominant lung cancer type globally *(3)*. Epidemiologic data suggest that filters are likely to have contributed to this increase. This pattern is attributed to deeper inhalation from filtered cigarettes and sustained cigarette consumption because of consumer's misperception of "safer" smoking with filters *(4,5)*. Over the same time overall lung cancer mortality risks associated with smoking (i.e. mortality rates for smokers and former smokers compared with those of non-smokers) increased, despite reductions in smoking prevalence and widespread adoption of filtered cigarette smoking. It is worth noting that the overall population risks of smoking have not decreased since the introduction of filters. Therefore, many researchers and public health advocates consider filters on cigarettes to be a deceptive technology that have facilitated continued smoking, misleading consumers into believing that they are smoking a less harmful cigarette while not reducing the overall harms of smoking*(2,6,7)*.

Although various materials have been used to make filters, almost all filters today are made of plastic, specifically cellulose acetate *(8)*. Thus, commercial cigarettes are essentially single-use plastic consumer products. The European Union, in its Single-use Plastics Directive of 2019 *(9)*, refers to filters as "single-use plastics that contain plastic and are commonly littered". Concern has arisen about the environmental impacts of this poorly degradable biopolymer, as trillions of cigarette butts are discarded annually *(10)*. The sheer quantity of these butts places them among the most-collected items of trash in urban and beach environments and qualifies them as a public nuisance *(11)*. In addition, discarded cigarette filters may persist for up to 10 years in the environment, suggesting long-term environmental consequences of this pollution *(10)*. Under various conditions, the discarded filters slowly degrade into microplastics that are likely to contain many of the 7000 chemicals in cigarette smoke. Some of these chemicals are environmentally toxic, and at least 70 are carcinogenic to humans and/or animals *(12)*. In laboratory studies, cigarette butts leach out chemicals, including nicotine, tobacco-specific nitrosamines (TSNA), plasticizers and heavy metals, and these leachates have been shown to be toxic and lethal in a wide variety of microscopic, animal and plant life *(13)*.

Environmental organizations have advocated for a ban on filters as a pollution prevention strategy *(14,15)*, in alignment with Article 18 of the WHO FCTC, which addresses protection of the environment and of human health in relation to the environment. In relation to Article 18, at the tenth session of the COP, decision FCTC/COP10(14) recognized "that plastic cigarette filters

are unnecessary, avoidable and problematic single-use plastics that are widely spread in the environment" *(16)*. In addition, a ban on filters would be consistent with Articles 9 and 10 of the WHO FCTC and the partial guidelines for their implementation, which recommend regulation of all design features that increase the appeal and attractiveness of tobacco products *(17,18)*.

5.1.1 Scope and aim

This report provides updated scientific information and considerations for regulatory and policy action on cigarette filters. We briefly review the history, types, effects on the attractiveness, addictiveness and toxicity of cigarettes, and misconceptions about cigarette filters. Next, we describe the concern about the chemical and plastic toxicity of cigarette filters, including the implications of environmental contamination for human health and ecotoxicity, issues related to filter biodegradability and recycling schemes and tobacco industry efforts to influence policies and the public regarding filters and the environment. Finally, we review opportunities for product regulation, design changes or sales restrictions related to filters, other single-use tobacco and nicotine products and accessories, in accordance with WHO FCTC Articles 9, 10 and 18.

5.1.2 Methods

This report benefits from recent work for WHO FCTC Decision FCTC/COP10(14): Implementation of Article 18 that address the environmental impacts of tobacco throughout the lifecycle of cultivation, manufacture, distribution, use and post-consumption disposal *(16)*. Literature searches were conducted between October and December 2024 for peer-reviewed literature on filters with phrases including "cigarette filter", "cellulose acetate filter", "filter ecotoxicity", "safe cigarettes" and "lung adenocarcinoma". During the review, additional papers were included to address pertinent issues. Robert N. Proctor's book, Golden Holocaust *(19)*, specifically Chapter 19, provided several important reference materials. Court cases, news media and various industry and public health websites on tobacco products were reviewed, particularly (https://cte.sdsu.edu/), (https://www.tobaccotactics.org/) and (https://www.industrydocuments.ucsf.edu/tobacco/). Reports were also obtained by "snowball sampling", accessing publications found to be relevant in reference sections of the articles examined. This document also draws substantially on a report of the Belgian Superior Health Council *(20)* and the open-access document, Tobacco product waste in California: a white paper, Appendix B1 *(21)*.

5.2 History, marketing and types of filters

5.2.1 Development and introduction of cigarette filters

Filters were first used in the 1860s to keep loose tobacco out of smokers' mouths *(22)*. In the 1930s and 1940s, however, they were marketed to protect smokers from the "poisons" of smoking *(19)*. They were usually composed of paper, wool or cotton; test materials included silica gel, cellulose and porcelain. Filtered cigarettes displaced unfiltered cigarette sales when the adverse health effects of smoking began to be discussed in the 1940s and 1950s. By the mid-1950s, scientific evidence implicated cigarettes as a key contributor to the increasing burden of lung cancer *(5)*. In 1955, Sir Richard Doll identified several carcinogens in cigarettes, including arsenic, 3,4-benzopyrene and radioactive potassium *(23)*. An internal document from 1952 by the Brown and Williamson Corporation revealed that their research team had detected the carcinogen benzo[*a*]pyrene in tobacco smoke *(24)*. R.J. Reynolds' research director confirmed in 1959 the presence of carcinogenic polycyclic hydrocarbons in tobacco smoke *(25)* and concluded that, "it is in the best interest of consumers for these compounds to be eliminated from tobacco smoke". Philip Morris' vice-president for science and technology reported a list of 40 carcinogens in tobacco smoke in 1961 and recommended that the levels of these compounds be reduced so that cigarettes would be "medically acceptable" *(26)*. Tobacco companies increasingly sought ways to reduce carcinogens, although these internal reports were not made public because the industry did not publicly acknowledge the presence of carcinogens in cigarettes *(27)*.

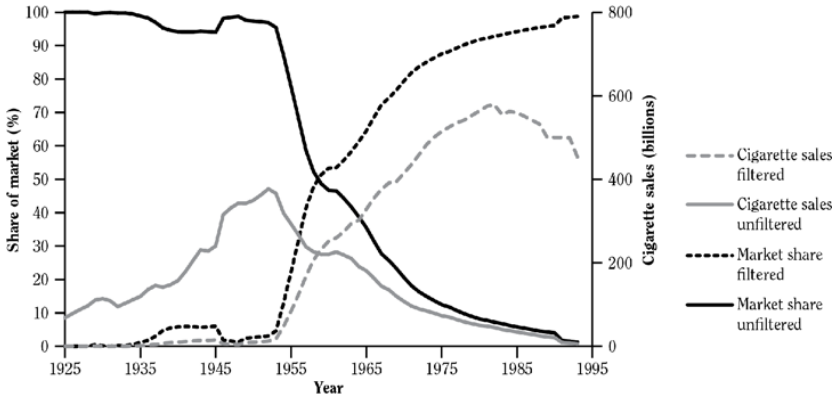
5.2.2 Marketing and consumption patterns of filtered cigarettes

In response to both internal and external research on the potential and real health consequences of smoking, cigarette companies expanded their marketing to suggest that cigarettes could be made safer by filters *(10)*. In 1951, only 1% of cigarettes on the US market had a filter; however, by 1958, almost half included filters, including Lorillard's Kent cigarette which had a filter containing crocidolite asbestos, a carcinogen *(19)*.

The industry's overall shift to filtered cigarettes continued into the 1960s because of two important events. First, in 1962, the United Kingdom's Royal College of Physicians published a report, Smoking and Health *(28)*, which highlighted the link between smoking and lung cancer and other diseases. Secondly, the US Surgeon General's Advisory Committee on Smoking and Health published their first Report on the Health Consequences of Smoking in 1964 *(29)*, citing evidence from more than 7000 articles related to smoking and disease to conclude that cigarette smoking is a cause of lung cancer and laryngeal cancer in men, a probable cause of lung cancer in women and the most important cause of chronic bronchitis. These reports received enormous press attention and fuelled the shift in tobacco

industry marketing to emphasize the value of smoking filtered cigarettes. In the USA, annual per capita cigarette consumption increased substantially during the 1950s and 1960s, as filters became the norm (Fig. 5.1). After publication of the aforementioned reports, per capita consumption decreased while use of filtered cigarettes became almost universal *(5)*; globally, more than 90% of the commercial cigarette market is filtered cigarettes *(2, 8)*. The tobacco industry also recognized that, by adding a filter to a cigarette, less tobacco was required to maintain cigarette length; this reduced the cost of manufacturing cigarettes from that when the finished product contained only tobacco *(19)*. The global cigarette filter market size was valued at US$ 38.19 billion in 2023 and is projected to reach US$ 65.61 billion by 2031 *(30)*.

Fig. 5.1. Market share and total annual cigarette sales of filtered and unfiltered cigarettes in the USA, 1925–1993



Source: National Center for Chronic Disease Prevention and Health Promotion *(5)*.

5.2.3 Types of cigarette filters

Almost all commercial cigarette filters are now made of cellulose acetate, a plant-derived plastic, with paper, plasticizers (triacetin and diacetin) and sometimes activated charcoal and flavours *(8)*. Numerous chemical companies around the world, in cooperation with the tobacco industry, manufacture filters. Although many manufacturers advertise eco-conscious filters, cellulose acetate is still the dominant component.

Other components that have been included in filters include flavourings, colourings and carbon. Flavour accessories, including capsules, threads and drops, are often used to circumvent flavour bans by adding flavours to otherwise unflavoured tobacco products *(31)*. Smokers can crush embedded capsules to release flavours *(32)*, which were initially menthol-flavoured but now include other flavours that are attractive to younger consumers. Flavoured threads have been added to the filter itself to increase appeal and to differentiate brands of cigarettes *(33)*.

Activated charcoal has been added to cigarette filters as a marketing tactic by the industry to "reduce volatile compounds in mainstream smoke"; however, there is no information about the health impacts of alternative cigarette filter materials such as charcoal.

5.3 Effects of filters on smoke emissions, smoking intensity and health

Filters and subsequent product modifications such as filter ventilation and activated charcoal were marketed for decades as "light" and "low-tar" to suggest that they reduced smoking-related health risks *(34)*. Machine-measured tar and nicotine exposure do not, however, reflect the true risks of smoking because of the variability of inhalation and compensatory smoking by people who smoke *(7)*. The addition of filters and other attempts to reduce machine-measured nicotine and toxicant emissions to alleviate smokers' health concerns may have delayed quitting and/or increased cigarette use.

5.3.1 Effects of filter ventilation

Much of the deception about reduced risks of smoking was related to introduction of filter ventilation, a filter modification that lowered the tar, nicotine and carbon monoxide (TNCO) levels measured by the ISO machine-based method (ISO 3308:2012) *(35)*. Small holes in the filter allow dilution of smoke during puffing. As many smokers try to extract sufficient nicotine to maintain smoking "satisfaction", they may voluntarily or inadvertently obstruct the vents, puff more deeply, and/or increase the number of cigarettes they smoke per day (so-called "compensatory smoking") *(7)*. Thus, the ISO method of machine smoking provides underestimates of actual human exposure to TNCO and other smoke constituents, and machine-measured reductions in toxicants and nicotine (the benefits of which were touted as "light" and "low tar" filtered cigarettes) do not reduce the harms of smoking *(35)*. Health Canada and WHO recommend testing methods that more closely approximate human smoking intensity to measure smoke emissions *(35)*.

5.3.2 Effects of charcoal filters

Hearn et al. *(36)* found that, under ISO machine-smoking conditions, charcoal-containing filters could remove some phenols, TSNA and lower-molecular-weight PAH *(36)*. The more dangerous, higher-molecular-weight PAH, such as benzo[*a*]pyrene, were not removed. Polzin et al. *(37)* found that a charcoal additive can reduce the levels of some compounds (e.g. tar, nicotine, carbon monoxide, volatile organic compounds) from machine-generated smoke; however, the effect depended on the amount of charcoal and on smoking topography (smokers' behaviour, such as puffing, inhalation and puff intervals). Under realistic human

smoking conditions, the charcoal can become saturated *(37)*. Nonetheless, smokers perceived charcoal-filtered cigarettes as less risky *(38)*. R.J. Reynolds has introduced charcoal-filtered Sky, a variant of their Natural American Spirit brand that is associated with misperceptions of health benefits *(39,40)*. In surveys, 28% of customers believed that Sky was less harmful than other cigarettes, and 38% believed that it exposed users to fewer chemicals. Charcoal filters appear to support such false beliefs in risk reduction and thus increase the appeal and attractiveness of cigarettes *(39)*.

5.3.3 Health implications of filters

Cigarette filters may have contributed to an overall increase in cigarette-caused mortality. Chapter 6, on cancer, in the US Surgeon General's Report in 2014 *(5)* extensively reviews how changes in cigarette design, including tobacco chemistry, the filter and its ventilation, have changed lung cancer mortality patterns. The risk for mortality from lung cancer associated with smoking (i.e. mortality rates of smokers and former smokers in comparison with that of non-smokers) has increased over time, despite reductions in smoking prevalence and adoption of filtered cigarettes. For example, the relative risks of death from lung cancer for women who were current smokers as compared with women who had never smoked were 2.73 in the 1960s, 12.65 in the 1980s and 25.66 in contemporary cohorts; the corresponding relative risks for male current smokers, as compared with men who had never smoked, were 12.22, 23.81 and 24.97, respectively *(41)*. In addition, the incidence of adenocarcinoma of the lung increased over the time that filters became widespread. This cell type of lung cancer occurs in the periphery of the lung, and the increase in its incidence is attributed to higher exposure of the lung periphery to smoke carcinogens because smokers inhale more deeply when the cigarette has a filter and especially a ventilated filter *(42)*. The evidence is deemed sufficient to conclude that the increased risk of lung adenocarcinoma among smokers has resulted from changes in the design of commercial cigarettes and in the tobacco types used in cigarettes since the 1950s. There is also suggestive evidence that ventilated filters and increased levels of TSNAs in modern cigarettes contribute to the increased risk of adenocarcinoma mortality, particularly among women *(4)*.

While the evidence for the potential role of filters in the increased prevalence of lung adenocarcinoma among smokers is substantial, the risk for this tumour also increased in nonsmokers during the same period, suggesting a potential contribution of environmental factors. Smoking of filtered or unfiltered cigarettes is a causative risk factor for any cell type of lung cancer, although the incidence rates of squamous-cell and small-cell types have decreased since filters and other cigarette modifications were introduced in the 1950s *(43,44)*. The higher risk for these cancers of people who smoke unfiltered cigarettes might have been due to greater exposure of the proximal lung (with shallow inhalation) to more

carcinogenic and genotoxic smoke *(45–49)*. Other earlier studies also show an increased risk for cancers with unfiltered rather than filtered cigarettes *(44,50–52)*. The results of these and more recent reports may, however, have been affected by various confounding factors, including cigarette type, amount of tobacco product, differences in socio-economic status and access to health care or to differences in the smoking topography of unfiltered cigarette users due to the harshness of unfiltered tobacco smoking. In addition, there is more tobacco in unfiltered than in filtered cigarettes; however, the extent to which the additional tobacco is usable by a consumer could be a factor in comparisons of the risks associated with smoking filtered and unfiltered cigarettes *(53)*. Despite these uncertainties, it is certain that the overall population risks of smoking any type of cigarette have not decreased since changes were made in commercial cigarettes. Therefore, continued smoking cessation interventions and other MPOWER measures *(54)* should be actively pursued, with a filter ban, to prevent the continued deception and devastation of smoking-attributable diseases.

5.4 Perceptions of cigarette filters

5.4.1 Misconceptions of the effectiveness of filters in reducing human harms

It is clear that cigarette companies sustained their sales in the 1950s and 60s by strategic advertising and concerted efforts to ease concern about the health risks of smoking. They received free advertising in widely read lay publications *(55)* and were able to advertise in professional journals promoting filters' efficacy in reducing "tar and nicotine" *(19)*. Smokers and some health-care professionals believed that the industry's claims of lower tar and nicotine yields would reduce the risk of disease from smoking. Although most smokers (60%) are unaware of filter ventilation, they consider that the "lightness" or "mildness" experienced when smoking cigarettes with a ventilated filter make them less harmful *(56)*. Smokers of higher ventilation filters perceived less harm than smokers of lower ventilation filters *(57)*. Ventilated filters result in more intense puffing, which likely contributed to the changing pattern of lung cancer cell type as filters became normalized *(4)*.

"Light", "low tar" and "mild" became key advertising messages, despite growing evidence of increased risks for lung cancer and other diseases, even with lower machine-measured TNCO yields *(6)*. Use of these terms is now prohibited in most countries under regulations pursuant to Article 11 of the WHO FCTC on packaging and labelling of tobacco products *(58)*.

5.4.2 Public knowledge about filters and attitudes towards regulatory policies

The public is poorly aware that overall health risks are not reduced by smoking filtered rather than unfiltered cigarettes *(59)*. Several reports of surveys in adults and youth have shown lack of knowledge about the plastic composition of filters (e.g. in the USA, > 70% of adults *(60)* and > 57% of youth *(61)*). A representative

household survey in 2019 of the German population aged ≥ 14 years indicated that the majority of both smokers and non-smokers did not know that cigarette filters were made of synthetic materials *(62)*. In all four countries (Australia, Canada, England and the USA) surveyed in the International Tobacco Control Policy Evaluation Project *(59)*, 75% of adults who smoked believed that removal of filters would make cigarettes more harmful, and belief that doing so would make cigarettes much more harmful was the strongest predictor of opposing a filter ban. A survey among US adults found that a belief that filters make it easier to smoke was associated with less support for a filter ban *(60)*. A survey in Netherlands (Kingdom of the) showed that more non-smokers (63%) than smokers (35%) would support a filter ban *(63)*.

5.5 Environmental impacts of discarded cigarette filters

5.5.1 Chemical toxicity of cigarette butt waste

Studies of urban runoff, wastewater, drinking-water sources and beach environments and the role of cellulose acetate filters in plastic environmental pollution indicate that, as filters trap some harmful chemicals, these can leach[1] into aquatic and terrestrial environments. Many of the toxicants found in cigarette smoke (e.g. nicotine, TSNAs, PAHs) are environmental pollutants that have been detected in leachates from tobacco product waste (TPW) *(64)*. Nicotine trapped by filters rapidly leaches from cigarette butts into aquatic environments, contaminating water at levels that are toxic to living organisms *(13,65–71)*. Additionally, cigarette butts leach low-molecular weight PAHs *(72)* and various toxic metals *(73,74)*. Cigarette butts could be categorized as hazardous waste owing to the presence of nicotine and other toxic chemicals listed as hazardous by regulatory agencies *(75,76)*. Little research has been conducted on the toxicity of unfiltered cigarette butts, but it is likely that the tobacco remnants of unfiltered cigarette butts will leach toxic chemicals as well. These remnants are, however, likely to biodegrade fairly quickly (2 months to 2 years), depending on the environment in which they are discarded and conditions including microbial characteristics, moisture and sunlight *(77)*.

5.5.2 Plastic pollution from cigarette filters

A cigarette filter comprises 12 000–15 000 individual cellulose acetate strands *(8)*. When cigarette butts are discarded into an aquatic or terrestrial environment, these fibres can detach, fractionate and disperse. A typical filter releases approximately 100 microfibres per day, most of which are < 0.2 mm in width *(78)*. Cellulose acetate has been identified in studies of urban water runoff *(79)*, and laboratory

1 "Leaching" is a term used in environmental sciences to refer to a liquid containing dissolved or incorporated harmful substances that may enter the environment.

studies provide evidence of the potential ecotoxicity of microfibres derived from cellulose acetate cigarette filters. Belzagui et al. *(78)* found that the breakdown of a smoked filter into microfibres induced substantially more toxicity in water fleas than that of an intact filter. It is not known whether the toxicity was due directly to microplastics per se, to tobacco chemicals released from the microplastics as the filters disintegrated or to some combination of these pollutants.

5.5.3 Biodegradability of filters

The tobacco industry has been aware of environmental concern about the poor biodegradability of cellulose acetate filters for several decades *(80)*. Bonanomi et al. published one of the few peer-reviewed scientific studies on the biodegradability of cigarette butts *(77)* and reported that, after 2 years of biodegradation, the average mass loss of cigarette butts was only 37.8%. The poor degradability of cigarette butts was attributed to the resistance of the cellulose acetate filter to microbial activity due to acetylation. When macerated butts were placed in a functional compost environment, 90% of cellulose acetate in the compost decomposed within 180 days (meeting the ISO standard for biodegradability *(81)*). Usually, however, discarded butts infrequently end up in a functional compost, and it is unlikely that infrastructure to collect and compost trillions of discarded butts would be feasible or safe. In addition, contamination of the compost with the chemical toxicants and carcinogens present in spent filters would present a challenge to its further use.

Given growing concern about discarded plastic cigarette filters, "biodegradable" filters could be used by the industry as a tactic to appear "eco-friendly" as part of their corporate social responsibility strategy *(34,82)*. Tobacco industry documents suggest that biodegradable filters would offer "outdoor convenience" by "eliminating" litter and allow smokers "to litter without guilt" *(83)*. Such products are already being marketed *(84)*, including filters made of natural materials such as hemp, cotton and wood pulp *(85)*, unbleached paper *(86)* and containing plant seeds *(87)*. None of these products has been evaluated for ecotoxicity, but it is likely that the same chemicals detected in cellulose acetate filters would leach from any type of cigarette filter. Products labelled "eco-friendly" will be used mainly as a marketing strategy to appeal to smokers who feel guilty about discarding plastic filters *(83)*. Filters (even if biodegradable) contribute to a continued misperception that filtered cigarettes are "safer" and may continue to provide a "smoother", more palatable smoking experience that can encourage progression from experimentation to sustained use and result in more intensive puffing. Emerging evidence suggests that promoting tobacco products as eco-friendly can lead to inaccurate perceptions of harm and addictiveness *(88)*. In addition, although biodegradable filters would decrease the micro-plastic problem, the discarded filters would still leach the contaminants captured by them during smoking and contaminate the environment when discarded

5.5.4 Recycling schemes

Marinello et al. *(89)* reviewed 37 publications describing approaches to recycling cigarette butts and categorized them according to output products. Although multiple studies have addressed reprocessing of cigarette butts, there has been no large-scale evaluation or experimental application of such products. Implementation of recycling schemes is unlikely to be feasible on a large scale, as collection of cigarette butts for commercial recycling would require significant logistics for collection, storage and transport. Collection and recycling schemes have so far been supported by the tobacco industry through environmental and private sector affiliates in an attempt to greenwash these ineffective TPW interventions *(90,91)*. An important consideration is the toxicity of both the cigarette butt substrate and the potential toxicity of the outputs and/or the by-products of recycling. Smoked cigarette butts contain toxic compounds, and recycling them will not necessarily remove the toxicity, which could lead to contamination of end products and more widespread exposure.

5.5.5 Human health implications of discarded cigarette butts

While trillions of butts are discarded each year, perhaps only a few million are collected and disposed of. Thus, there is growing concern that accumulation of the chemicals, plastic remnants and other components of TPW over decades will have broader ecosystem impacts and subsequently long-term human health impacts resulting from environmental pollution with TPW.

5.5.5.1 Bioaccumulation

Researchers have identified approximately 800 chemical constituents in fresh and saltwater cigarette butt leachates. Nicotine was the most abundant chemical, followed by the plasticizers diacetin and triacetin. Several of these chemicals were recently found to bioaccumulate in rainbow trout and mussels (potential human food sources) *(92)*. The leachates of smoked cigarettes were genotoxic and cytotoxic in these organisms, suggesting a potential risk to human health on consumption of exposed biota.

5.5.5.2 Cigarette butt ingestion

Novotny et al. *(93)* reviewed data from poison control centres on emergency room admissions after accidental ingestion of tobacco products, including filters. Cases of nicotine poisoning due to consumption of cigarette butts were uncommon; however, both humans and animals may consume butts and show serious gastrointestinal, central nervous system and cardiovascular signs. A recent report *(94)* indicated potential ingestion of heated tobacco sticks by children, suggesting a similar problem as with cigarette butts.

5.5.6 Harm to ecosystems

Plastic cigarette waste degrades environmental quality by fouling beach environments, despoiling public lands such as parks, and degrading neighbourhoods and public spaces. Such environmental impacts are a threat to the delivery of ecosystem services, defined as the benefits derived by humans from intact ecosystems, such as food supplies, water and waste purification, medications and cultural and aesthetic services such as tourism and recreation *(95)*. As environmental microorganisms catalyse key biogeochemical cycles (e.g. carbon, nitrogen, phosphorus, sulfur and iron) and ecosystem services (e.g. waste attenuation and agricultural food production), more research is necessary to document any longer-term impacts on ecosystems, beyond laboratory settings *(91)*. One recent study identified urban stormwater runoff as a potential source of nicotine and cotinine pollution in a protected reserve, implicating tobacco product litter and human tobacco use as contributing factors *(96)*. A study of surface area storm-water runoff found cellulose acetate as the predominant identified polymer, although identification of the source of the cellulose acetate was not technically possible *(79)*. Clean-up and collection of discarded TPW, whether by waste management services or by voluntary groups, are one means to reduce pollution, although it might present health risks due to exposure to hazardous chemicals in filters and is time-consuming, labour-intensive and ultimately insufficient *(97,98)*. Such activities could never collect sufficient TPW to meaningfully reduce the trillions of butts discarded each year *(99)* and are furthermore often co-opted by the tobacco industry for greenwashing *(100,101)*.

5.6 Summary

Widespread use of cigarette filters has not reduced the population-level adverse health risks of smoking. The risks for cancers, cardiovascular disease and pulmonary disease due to smoking have not decreased during the decades during which filters became normalized *(41)*. Instead, cigarette filters have been used as a misleading marketing tool by the tobacco industry to counteract concern about the adverse tobacco-related health effects *(12,34)*. The commercial cigarette filter has even been called the "...deadliest fraud in the history of human civilization" *(102)*. Cigarette filters have limited capacity to significantly reduce human exposure to toxic tobacco chemicals and particulates in tobacco smoke but can provide a false sense of security to the user. Discarded filters also contribute significantly to environmental pollution, as they trap particulates and toxicants that readily leach into water and soil, are not usually biodegradable and can release microplastics as they degrade. As an environmental concern, the filter fits the description of a non-essential, widespread, potentially toxic single-use plastic consumer product that could be eliminated in a source reduction strategy *(103)*.

5.7 Conclusions

- The use of filters likely have contributed to the increased incidence of lung adenocarcinoma and the sustained population risks for lung cancer mortality.
- Filters increase the palatability and appeal of cigarettes, contribute to consumer misconception that they reduce health harms and represent a deceptive marketing gimmick.
- Filters are a major contributor to post-consumption tobacco waste, are environmental contaminants due to the leaching of toxic chemicals and microplastics and impose economic costs for waste mitigation.
- The evidence of both public health and environmental harm due to filters warrants immediate action. It is critical that the public health community not allow the industry to co-opt environmental policies for their reputational gain.

5.8 Research gaps, priorities and questions

- Additional research is needed on effective communication strategies to address misconceptions about the function, composition and lack of effectiveness of cigarette filters in reducing the harms of smoking.
- More research is needed on the effects of filtered (versus unfiltered) cigarettes on quitting, initiation and consumption. The results of a pilot trial suggest that smokers who switched to unfiltered cigarettes for 2 weeks smoked fewer cigarettes per day and experienced less satisfaction from their smoking but showed no significant difference in cotinine or in urinary biomarkers of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol *(104–106)*.
- More research should be conducted on the ecotoxicity of tobacco product waste, including unfiltered cigarette butts, on wildlife and human health, beyond laboratory studies, to address short- and long-term ecological impacts.
- Surveillance systems to monitor changes in the market, changes in consumer behaviour and compliance with regulations should be strengthened. This will not only increase a country's enforcement response but will also provide information to counter industry claims and arguments.

5.9 Regulatory options regarding cigarette filters

5.9.1 Policy options

The scale of the problem of cigarette filters suggests that structural solutions are required, including a range of policy options. Extended regulatory policies on tobacco products are necessary to mitigate both the adverse health effects of filtered cigarette smoking and the environmental pollution by discarded cigarette butts, product packaging, other tobacco products and nicotine products. Such policies may include the application of "extended producer responsibility" schemes, designed to hold tobacco manufacturers accountable for the post-consumer waste generated by their products, including filters and packaging. Tobacco control advocates should join with environmentalists to reduce or eliminate this source of environmental pollution in cross-disciplinary action *(107)*. Public health researchers, advocates and some jurisdictions have supported a ban on filtered cigarettes to reduce their attractiveness and consumption *(12,42,108)*. The most direct option would be to ban the sale of filtered cigarettes. The expected outcome of such a ban, which would reduce tobacco and nicotine product use, would meet both public health and environmental protection goals. A ban on filters would also likely be beneficial for the environment, by eliminating a major source of macro- and microplastic pollution.

5.9.2 The current regulatory environment

WHO FCTC Article 9 addresses the testing and measurement of the contents and emissions of tobacco products and their regulation. WHO FCTC Article 10 addresses disclosure of information on contents and emissions to government authorities and the public. Hence, any recommendation for regulating filters would be supported by implementation of these articles *(18)*. Article 12 calls for education, communication, training and public awareness, which is highly relevant and critical to address misinformation and the "filter fraud" narrative. Article 18 of the Convention states that Parties have a duty to protect the environment with regards to tobacco cultivation, manufacture and disposal *(16, 17)*, and, at the 10th session, Parties adopted a decision on implementation of WHO FCTC Article 18 (FCTC/COP10(14)), which urges Parties to coordinate their efforts to address the plastic waste of tobacco products and electronic devices in relation to national policies and international treaties *(16)*. In addition, Parties called for an expert group to address WHO FCTC Article 19, which considers actions to deal with the criminal and civil liability of the tobacco industry, including compensation where appropriate *(109)*. Environmentalists and public health advocates who attended negotiations for a proposed United Nations Environment Programme Plastics Treaty have advocated for filters to be included on a list of single-use plastics that could be banned outright as non-essential, harmful and widespread plastic

pollutants *(110)*. The European Union Single Use Plastics Directive, 2019, does not ban cigarette filters but regulates them in the category of "single-use plastics that contain plastic and are commonly littered" and places the responsibility for addressing filter waste on tobacco companies *(9)*. The Belgian Superior Health Council recommended a ban on cigarette filters in 2023 *(20)*, concluding that "cigarette filters have no proven benefits in preventing adverse health effects of smoking", "cause large environmental pressure" and "sees no solution in advocating 'green' biodegradable filters".

5.10 Main recommendations

- Extend public education on cigarette filters as a health and environmental hazard, including on package warnings and point-of-sale advertising. Assure dissemination of information on misconceptions about the composition of filters, that they do not protect against many of the risks of smoking and that their main function is to sustain cigarette consumption.
- Implement a ban on filters. If an immediate ban is not feasible, implement a plan to phase them out. Information campaigns should provide a clear explanation for the rationale of the ban, build public support and ensure that the industry does not co-opt this policy measure for their reputational gain. Smokers should be supported in quitting with approved cessation tools of proven efficacy and safety.
- A ban on filters, in the context of comprehensive regulation of tobacco products in line with the WHO FCTC (e.g. Article 2.1 on forward-looking interventions, Articles 9 and 10 on product regulations, Article 18 on concern for the environment and Article 19 on the accountability and liability of the tobacco industry), will require broad collaboration among different disciplines and leveraging of ongoing global frameworks and initiatives.

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6. Evolving design, additives and accessories for cigarettes and effects on addictiveness, attractiveness and toxicity

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Contents

Abstract
6.1 Introduction
6.2 Methods
6.3 History of important cigarette design variations
6.3.1 Elasticity
6.3.2 Filters
6.3.3 Filter ventilation
6.3.4 Menthol
6.3.5 Charcoal
6.3.6 Slim and superslim cigarettes
6.3.7 Roll your own
6.3.8 Pseudocigarettes
6.4 Emerging issues relevant to cigarette design
6.4.1 Synthetic coolants to replace menthol
6.4.2 Synthetic nicotine
6.4.3 Nicotine analogues
6.4.4 Substitute fillers
6.4.5 Filter (flavour) capsules
6.5 Aftermarket modifiers of commercial cigarettes
6.5.1 Flavour cards or inserts
6.5.2 Filter modifiers
6.5.3 External filters
6.5.4 Smoking devices
6.6 Discussion
6.7 Recommendations
6.7.1 Short-term
6.7.2 Medium- and long-term
References

Abstract

Although the WHO FCTC entered into force more than two decades ago, cigarette brands and line extensions continue to proliferate globally. This briefing paper highlights emerging issues in the cigarette marketplace that may have implications for cigarette addictiveness, attractiveness and/or toxicity. Data were obtained from the published literature in systematic searches of the US National Library of Medicine's PubMed database with relevant keywords. In addition, industry activity was examined from tobacco industry documents, tobacco science literature, the Tobacco Reporter, publicly traded company disclosures and patents for cigarette design elements. We provide historical examples of methods used by the tobacco industry to manipulate the addictiveness, attractiveness and toxicity of cigarettes by changing product characteristics such as filters, filter ventilation, charcoal and menthol. We also describe current evolution in cigarette product design that may be used for certain purposes or to circumvent regulations, such as slim cigarettes, synthetic coolants to replace menthol, substitute fillers, flavour capsules and charcoal filters. Similarly, changes in non-cigarette product characteristics, such as inclusion of synthetic nicotine, nicotine analogues and substitute fillers, could apply to cigarettes. We also discuss modifiers of commercial cigarettes after marketing, such as flavour cards, filter modifiers and external filters and smoking devices. Many of these changes enhance the addictiveness and appeal of cigarettes but do not reduce their toxicity. Clear, comprehensive definitions are required in regulation of cigarettes, tobacco and nicotine products. WHO Member States must be diligent in formulating comprehensive regulations to ensure that emerging designs of cigarettes and related products do not enter the market and reverse trends as the prevalence of cigarette sales and smoking prevalence decreases.

Keywords: cigarette; filter; accessories; design; flavour; charcoal; policy

6.1 Introduction

Articles 9 and 10 of the WHO FCTC address the regulation of tobacco products, specifically with respect to addictiveness, attractiveness and toxicity. Article 9 directs the Conference of the Parties to "…propose guidelines for testing and measuring the contents and emissions of tobacco products, and for the regulation of these contents and emissions." WHO FCTC Article 10 deals specifically with the issue of product disclosures, from manufacturers to governments and by governments to consumers. Implementation of these articles has been slower than that of other aspects of the treaty, owing in part to the complexity of the issues involved in product regulation *(1,2)*.

Cigarette brands and sub-brands continue to proliferate globally, more than two decades after the WHO FCTC entered into force. Why? Tobacco manufacturers

seek to maintain or grow their market share, which involves selecting product design features to achieve appealing sensory properties and adequate nicotine delivery and branding intended to attract specific target audiences *(3–12)*. Product characteristics affect their harmfulness, acute toxicity and experience of use, which are central to understanding patterns of use *(13)*. Design changes can influence users' perception of risk and self-reported experiences during use of a given product, such as perceived drug effects (satisfaction, withdrawal suppression, craving reduction), sensory experiences (e.g. smell, taste, trigeminal effects), outcome expectancy (e.g. stress reduction, relaxation, attention) and evaluation (liking, willingness to use again) *(14)*.

During the past decade, the attention of the tobacco control community has been drawn to new and emerging products, such as ENDS, HTP and nicotine pouches, due mainly to their adoption by youth (e.g. re-normalizing, potential gateways) and potential disruption of public health gains. These products have also, however, also distracted tobacco control from the continued presence of cigarettes in the marketplace, which continue to evolve with the accumulation of small changes, proliferation of line extensions and promotion. These accumulated changes may slow or reverse the rate of decrease in smoked tobacco use. An important means for shaping the future of tobacco use is consideration of how the tobacco industry might respond to restrictions on product contents and emissions by alterations in product design *(11,15,16)*. This briefing paper highlights emerging issues on the cigarette marketplace (including both manufactured and roll-your-own products), briefly summarizes the historical impactful (i.e. widely adopted), changes in cigarette design and design innovations that may have implications for the addictiveness, attractivity and toxicity of cigarette. This complements and adds to information briefs issued by WHO for 2025 World No Tobacco Day *(17–20)*.

6.2 Methods

Data were obtained from the published literature in systematic searches of the US National Library of Medicine PubMed database during October and November 2024 with relevant keywords (e.g. filter, cigarette, design, charcoal, flavour, capsule, synthetic, analog(ue), herbal, pseudocigarette, roll-your-own). We also searched tobacco industry documents on the site of the University of California at San Francisco Truth Tobacco Industry Documents collection (https://www.industrydocuments.ucsf.edu/tobacco/). We examined the tobacco science literature through searches in the Beitrage zur Tabakforschung International archive and the abstracts from the database of the Cooperation Centre for Scientific Research Relative to Tobacco, which contains much mainly industry-supported research. Industry activity was also examined from publicly traded company disclosures (e.g. stockholder annual reports). We searched for patents for cigarette design elements in Google Patents. We also examined patents issued

to or held by the major international tobacco manufacturers (e.g. Philip Morris International and Japan Tobacco International) or by major tobacco industry partners (e.g. Filtrona), which are considered as most likely to be integrated into cigarettes in the near term.

6.3 History of important cigarette design variations

Cigarettes have been changed significantly over the past 75 years *(11,12,21,22)*. Initial design innovations included introduction of reconstituted tobacco (tobacco leaves and stems combined with additives and processed into a paper-like material) and expanded tobacco (tobacco leaf treated to increase its volume per unit mass) to blends as well as cigarette paper of higher porosity *(22)*. An example is use of ammonia technology in cigarettes, in which ammonia salts are added to the tobacco to increase pH and thus change more nicotine into the free-base form. This is hypothesized to have a smaller role in increasing the availability and absorption of nicotine, as ammonia is considered to have only a small effect on nicotine bioavailability *(23,24)*. This additive is nevertheless to considered to have contributed significantly to Marlboro's dramatic growth during the 1960s and 1970s *(25)*. Camel's reformulation in the late 1980s and early 1990s (such as changes in humectants and other additives, addition of expanded tobacco to the blend, increased tobacco density) was used to reduce the perceived harshness as part of marketing of smoothness, which was instrumental in attracting US youth smokers *(10)*. Specific design features that have changed over time and their putative effects on addictiveness, attractiveness and toxicity are described below.

6.3.1 Elasticity

Nicotine is the major addictive substance in tobacco, and the industry has engineered cigarettes to deliver sufficient nicotine to maintain smokers' addiction through a range of design variations. Cigarette engineers coined the term "elasticity" to describe cigarette design that can deliver more nicotine than is measured in standard laboratory smoking machine tests (e.g. those of ISO), depending on how the product is used *(26)*. Manufacturers developed strategies to increase product elasticity *(26–29)*, which allow the smoker to maintain consistent exposure to nicotine with varying nicotine rating under testing conditions *(30–32)*. The process by which smokers take more nicotine from a cigarette than is registered in machine tests is known as compensation *(27,33–35)*.

6.3.2 Filters

In the 1950s and 1960s, in response to mounting health concerns, tobacco companies began to market filtered cigarettes in ways that implied a reduction in the quantities of toxic chemicals in smoke. Their marketing consultants objected to this strategy because it reminded smokers of the dangers of smoking cigarette

while attempting to provide reassurance. Although filters were ostensibly added to reduce tar and nicotine yields *(36)* and to mitigate concerns about smoking-related lung cancer *(27)*, cigarette filters do not eliminate the harm of smoking cigarettes *(27,37,38)* and may increase the appeal of smoking (alone or by including elements such as capsules) *(33,39,40)* and their toxicity, because the filter microfibres that can leach chemical toxins *(37,41,42)*. A fuller history of cigarette filters and their sequalae is discussed in Chapter 4.

6.3.3 Filter ventilation

The introduction of filter ventilation in the late 1960s was a significant shift in design, which eventually became a very common element in all brands *(43)*. Filter ventilation involves introduction of holes in the paper covering the cigarette filter, through which air is drawn when a puff is taken, diluting the mainstream smoke. The effective smoke concentration from a cigarette that has 25% ventilation is diluted to 75% of its original value, and the remaining smoke volume is replaced by air *(44)*. Ventilation is strongly correlated with Federal Trade Commission/ ISO "tar" and nicotine yields ($r > 0.70$) *(15,45–51)*. Ventilation is more commonly used in the Americas, European and Western Pacific WHO regions than in other regions, and areas with the highest average tar yields have the lowest average level of ventilation level *(52)*. Laboratory testing of cigarettes in international markets is consistent with the hypothesis of an association between the level of filter ventilation and country income, whereby vented cigarettes are more prevalent, with more ventilation in higher-income countries *(46,49,50,53)*. As countries become more affluent, the levels of education and awareness of health risks increase, and such brand variants are introduced onto the marketplace *(54,55)*. In China between 2009 and 2012, the reported "tar" level in 81 brand styles decreased by 7.9%, while that of ventilation increased significantly (by 31.7%) *(56)*. Vents in particular contribute to the perception of a lighter, milder smoke, which deceives smokers into believing that they are smoking safer cigarettes *(57–62)*. "Elastic" cigarettes facilitate compensation, and filter vents are the main design feature on which the industry relied to create elastic products *(63)*. Addition of ventilation to a cigarette filter generally decreases resistance to draw (also known as "pressure drop"), in effect facilitating larger, higher-velocity puffs, thus allowing a greater total volume of smoke to be drawn from a cigarette *(64)*. Filter vents may also be associated with increased levels of "free" nicotine, which may more bioavailable than the unprotonated form *(65)*. Although manufacturers and some public health authorities in the late 1960s and early 1970s were initially optimistic about lowering the standard level of tar in products, both laboratory and epidemiological studies indicate neither an individual nor a public health benefit of smoking cigarette varieties with lower than higher tar levels *(27,66,67)*. Moreover, low tar cigarettes appear to increase the prevalence of experimentation by new users and to delay

cessation *(68)*. The increase prevalence of adenocarcinoma of the lung observed in recent decades probably reflects greater exposure of the periphery of the lungs to smoke particles due to the addition of the filter and filter ventilation (e.g. deeper inhalation) and to use of higher concentrations of tobacco-specific nitrosamines in smoke from Burley tobacco in blended cigarettes (*69–74*).

6.3.4 Menthol

Tobacco companies have attempted to reduce the harshness of cigarette smoke by adding menthol or other characterizing flavours *(75–78)*. Menthol increases a product's appeal to potential users, particularly youth *(79,80)*, such that most tobacco users now start with menthol cigarettes or flavoured cigars *(81)*. Kreslake et al. analysed tobacco industry documents and found two kinds of menthol cigarette on the US market *(76)*. Some contain low levels of menthol and are designed to produce a "smooth" smoke *(82)*, whereas others contain higher levels of menthol to produce a "strong" smoke. The former are more popular among youth and are often used as "starter" products *(82)*, while the others are most popular with African–American males for whom the brand may be used as a distinct cultural identity *(77)*. The taste characteristics of American blend cigarettes (such as the inclusion of Burley) may influence the use of menthol to a greater extent than on those markets in which flue-cured cigarettes dominate. There is broad public support for removing menthol from cigarettes *(83)*, and most adults who smoke menthol cigarettes would prefer to quit smoking in response to such regulation *(84,85)*. A recent systematic review on the impact of menthol bans showed that nearly 25% of menthol smokers quit after the ban was implemented and that more menthol cigarette smokers quit smoking after the ban than non-menthol cigarette smokers. The review also showed that 12% of menthol smokers switched to other flavoured tobacco products, indicating the importance of a comprehensive accompanying ban of all flavoured tobacco products *(86)*.

6.3.5 Charcoal

Activated charcoal is commonly used in medical, industrial and consumer products as a purifier or detoxifier *(87)*. The charcoal cigarette filter was hypothesized to reduce the levels of volatile and semi-volatile toxicants in cigarette smoke *(38,88)*. Charcoal can be added throughout filters ("Dalmatian style") or as a concentrate in a cavity ("plug style") *(39)*. Some selective retention of smaller molecular weight compounds has been suggested *(89,90)*; however, it has also been shown that charcoal filters may result in inhalation or ingestion of polycyclic aromatic hydrocarbons on carbon particles, which could increase the risks to health *(42)*. The amount of charcoal used in the filters of cigarettes on the market today is not large enough to reduce significantly the smoke of volatile and semi-volatile compounds when cigarettes are smoked at normal puff velocity *(89,90)*.

Charcoal-filtered cigarettes have been available since the late 1960s, when Japan Tobacco International introduced Seven Stars *(91)*. They are most popular in Japan, Hungary, the Republic of Korea, the Russian Federation, Switzerland and Venezuela (Bolivarian Republic of) *(38,88,92)*. By 2004, nearly all filtered cigarettes sold in Japan had a charcoal filter *(91)*. Japan Tobacco International also sells Mevius (previously Mild Seven), which is popular in the Republic of Korea and other parts of Asia *(93)*. US brands include Lark, Tareyton and Parliament *(39)*. While charcoal filters have not been popular in the USA, Natural American Spirit, a leading US brand *(87,94)* that is claimed to be natural and organic *(95)*, has introduced a new style of cigarettes named "Sky". The company claims that the "charcoal filter mellows the taste of our whole-leaf tobacco, providing a smooth taste that's deliberately different" *(87)*. The brand has been shown to mislead consumers into believing that their cigarettes are a healthier alternative *(95)* by use descriptors such as "organic", "natural" and "additive-free", with nature-related imagery *(87,95–98)*. While Sky is not the first Natural American Spirit product that contains a charcoal filter, it is the first advertised to consumers with such a description and listing the ingredients as "tobacco and water "*(87)*, which may mislead consumers to believe that it is a harm-reduction product *(98)*.

6.3.6 Slim and superslim cigarettes

Cigarettes with narrower dimensions, introduced in the late 1960s in the USA (Virginia Slims), have typically been marketed to women, often with imagery and messaging associated with women's liberation or freedom *(99–101)*. At the height of their sales, in the early 1980s, Virginia Slims commanded over 3% of the US market, although its share fell rapidly thereafter. These products have been re-emerging globally since the mid 2010s. In Canada, the prevalence of use of slims among youth increased from 1.3% in 2008–2009 to 5.1% in 2012–2013 and proportionally larger increases among females and in youth aged 14–15 years who smoked *(102)*. Data on Chinese smokers suggest that as many as 38% were using slim cigarette *(103)*, women and people with a higher educational level being more likely to do so. In surveys among smokers in six EU countries, 21% of smokers viewed slims as less harmful, with moderate (18–33%) support for restrictions on slim cigarette sales *(104)*. Little published evidence was available that slim cigarettes expose smokers to meaningfully lower levels of toxicants, and most studies were based on estimates of exposure at filter and mouth level *(105–107)*. The measurable differences in emissions under ISO smoking conditions between slim and standard diameter cigarette imply compensatory smoking.

6.3.7 Roll-your-own

Regulatory loopholes might be exploited by sale of loose tobacco that users can roll into cigarettes with rolling papers (roll-your-own) or fill into cigarette tubes

(fill-your-own or make-your-own). Smoking such cigarettes results in the same exposure to toxicants as smoking factory-made cigarettes *(108)*, although roll-your-own tobacco may contain higher levels of humectants and sugars *(109)*. The prevalence of roll-your-own cigarettes varies widely by country *(110–112)*. Roll-your-own cigarettes are often less expensive than factory-made cigarettes, and the prevalence of their use may fluctuate with their price:tax ratio to that of factory-made cigarettes *(112,113)*. People who smoke roll-your-own cigarettes cite relative cost as a primary reason for choosing these cigarettes *(112)*. Roll-your-own cigarettes may be subject to fewer regulations than factory-made cigarettes, especially in low- and middle-income countries where the tobacco is grown locally *(110)*. Regulations to reduce the prevalence of tobacco smoking should cover a wide variety of tobacco and nicotine products rather than only factory-made cigarettes to ensure that people who smoke are less likely to adopt other forms of tobacco and nicotine.

6.3.8 Pseudocigarettes

The tobacco industry could circumvent regulations on cigarettes by promoting "pseudocigarettes", defined as products that resemble cigarettes but are classified differently legally. Such classifications may result in differential regulation and taxation for products that are functionally similar to cigarettes. For instance, small, "little" filtered cigars are similar in size, shape and design to conventional cigarettes but are typically wrapped in tobacco leaf (or a substance containing tobacco) rather than paper that does not contain tobacco. In the USA, these definitions have led to different regulations and taxes on these products, most of which are more favourable towards little cigars than to cigarettes, even though the toxicity of these products is essentially the same as that of cigarettes *(114)*. R.J. Reynolds documents from the 1970s indicate that Winchester, a little cigar, was designed for cigarette smokers and to be as similar to cigarettes as possible while avoiding bans on advertising and exploiting price and tax structures *(115)*. These products were advertised in ways that were appealing to cigarette smokers and blurred the lines between cigarettes and little cigars, by using, e.g. similar brand names, pack designs, pack size and physical characteristics *(114)*; cigarette smokers may have difficulty in distinguishing between these products *(116)*. Similarly, these products were developed in the USA to circumvent the ban on flavoured cigarettes by the US FDA in 2009 *(117)*. While there is no evidence of a problem with little cigars globally, these products are not specifically defined in the WHO FCTC, which may leave countries vulnerable to similar loopholes *(118)*. Pseudocigarettes are one example of a product used by the tobacco industry to blur the line between cigarette and non-cigarette (but cigarette-like) tobacco products to circumvent regulations and taxes.

6.4 Emerging issues relevant to cigarette design

6.4.1 Synthetic coolants to replace menthol

A recent development in the cigarette marketplace has been use of synthetic coolants as substitutes for menthol on markets in which menthol has been banned. A number of jurisdictions, led by Canada in 2015 *(119)* and the EU in 2020 *(120)*, have imposed bans on menthol in cigarettes. The USA prohibited use of menthol as a characterizing flavour in the final stages of rule-making, which was subsequently paused *(121)*. Some jurisdictions (e.g. Brazil, Canada) have banned use of menthol as an additive, whereas others (e.g. EU) have banned menthol as a characterizing flavour. In late 2022, the US state of California prohibited retail sales of cigarettes with characterizing menthol flavours, defined as "a distinguishable taste or aroma, or both, other than the taste or aroma of tobacco" *(122)*. Evaluation of menthol restrictions in Canada, the United Kingdom and elsewhere show that sizeable fractions of smokers (≥ 8%) have quit as a result of these restrictions, with little increase in illicit trade *(119,123–127)*. There are recognized limitations and potential loopholes in the term "characterizing menthol flavours". For example, manufacturers could evade the impact of the restriction by substituting other compounds for menthol, such as methyl salicylate (wintergreen), carvone and eucalyptol, which have recognizable odours. Synthetic compounds such as WS-3 and WS-23 can provide a cooling sensation without a characteristic odour or taste. WS-3 provides the cooling effect similar to that of menthol by binding to the same cell receptors *(22)*, although with potentially greater potency *(23)*.

Data on industry compliance with and evasion of such regulations are mixed. Marketing campaigns in California of re-branded cigarettes with "fresh" and "crisp" and "non-menthol" descriptors *(128)* may lead consumers to expect that the replacement products will deliver a similar cooling sensory experience *(129)*. Analysis of cigarettes sold in California *(130)* showed no menthol in any part of the tested cigarettes (labelling, tobacco filter or non-tobacco material) after introduction of the restrictions. The menthol in Newport and Camel brands appears to have been replaced by WS-3 *(130)*. Jabba and colleagues *(131)* found similar results and identified activation of the menthol or cool receptor, TRPM8, in smoke extracts of "nonmenthol" cigarettes.

In a recent overview of the policies of WHO Member States on additives conducted by WHO *(133)* at the end of 2022, 48 countries (25%) reported that they had a regulation to restrict menthol and its analogues, precursors and derivatives in cigarettes, eight of which were in the African Region, three in the Americas Region, one in the South-East Asia Region, one in the Western Pacific Region and the remaining 35 in the European Region. A further 50 countries (26%) reported having a policy that prohibits additives to increase the attractiveness or mask the harshness of cigarettes. Menthol restrictions could, however, result in new cigarette formulations containing synthetic coolants, providing a continued

consumer perception of a cooling sensation, despite the removal of menthol. The extent to which such substitution is occurring in other markets that have restricted menthol is unknown and should be studied more closely. A recent review of the use of coolants, organic acids, flavourings and sugars as additives indicates that regulation is designed to facilitate inhalation *(132)*. The toxicity of some of these compounds as used in cigarettes has not been adequately studied. California has since updated its definition of "characterizing flavour" to close this loophole, although the state effectively enforced the menthol ban before a legal definition was redefined *(133)*.

6.4.2 Synthetic nicotine

Nicotine exists naturally as two stereoisomers of *S*- and *R*-nicotine. Nearly all nicotine derived from tobacco plants contains *S*-nicotine (> 99%) and very low levels of the R isomer *(134)*. Manufacturers have, however, created both a synthetic form of *S*-nicotine and a racemic form that contains 50% *S*-nicotine and 50% *R*-nicotine *(134,135)*, both of which avoid regulations on "tobacco-derived products". In 2023, Berman et al. published a review on synthetic nicotine, commissioned by WHO *(136)*, which describes both synthetic *S*-nicotine and racemic nicotine, which have been observed mainly in ENDS, nicotine pouches and alternative nicotine delivery products (e.g. gums, toothpicks). While nicotine was first synthesized in 1904, tobacco industry documents show that British–American Tobacco considered using synthetic nicotine in the 1960s to increase the nicotine:tar ratio in cigarettes, although the proposal was not pursued *(136)*. Similar investigations were conducted by R.J. Reynolds and Liggett & Myers, and industry scientists continued to work on synthesizing pure *S*-nicotine *(136)*.

Since 2015, shortly after the US FDA began discussing extension of its regulatory authority to include ENDS, several companies emerged (Next Generation Labs, Zanoprima, Contraf-Nicotex-Tobacco) that manufacture and have filed patents for synthesis of *S*-nicotine and racemic nicotine, some of which have been found in ENDS marketed in the USA. These companies have noted "fewer restrictions on entering new markets" as a benefit of synthetic nicotine, suggesting that such products could be used by the industry to circumvent regulations. Synthetic nicotine products are also often promoted as containing "tobacco-free nicotine" *(137)*, which may be perceived as less harmful and more appealing than tobacco-derived nicotine *(138–140)*. One study suggests that nicotine pouches with *S*-nicotine deliver more nicotine to the user than racemic nicotine, although subjective tests of "liking" and withdrawal gave similar results, with more "bad effects" (not defined) reported with *S*-nicotine *(141)*. It is not clear whether the same results would be found for smoked products. To our knowledge, synthetic nicotine and racemic nicotine have not been found in commercially available cigarettes or in other tobacco plant-containing products.

6.4.3 Nicotine analogues

Nicotine analogues are chemically distinct from nicotine but are intended to mimic its effects. For instance, 6-methyl nicotine, also known as metatine and other brand names, such as Nixotine, Nixodine and Imotine *(142)*, appeared on the US market in 2023 in the product Spree Bar *(143)* and was extended to the nicotine pouch market in 2024 *(142)*. The compound has also been identified in ENDS liquids in Australia *(144)*. One nicotine pouch brand, Sett (founded in 2024), claims to include Ceretine and L-theanine in their product. The brand website describes Ceretine as "a proprietary tobacco-free alkaloid, designed to provide the same satisfaction as nicotine" and "a proprietary ingredient which is structurally similar, yet chemically distinct from nicotine. It is designed & verified to deliver similar effects to nicotine by binding to acetylcholine receptors". The claim is also made that it "supports a state of focus and alertness by promoting dopamine and acetylcholine production – thus providing a similar sensation and satisfaction to that of nicotine" *(145)*. These products also contain L-theanine, described as "an amino acid proven to reduce stress by promoting serotonin and dopamine production" *(142)*.

By 2025, limited independent scientific research had been conducted on nicotine analogues, and much of what was known came from industry documents or patents. One survey of California adolescents indicated that about 20% were aware of such products, and up to 10% had ever used them *(146)*. For instance, a patent assigned to Shanghai Lingnuo Biotech based on studies in humans claimed that 1 mg/mL of 6-methyl nicotine was as satisfying and produced a similar "throat hit" as 3 mg/mL nicotine, although the study was small (n=10), and was reported with few details *(147)*. A study in rats in vivo indicated that 6-methyl nicotine may be more toxic than nicotine *(143)*. Although no comparison has been published of the effects of 6-methyl nicotine and those of nicotine, a study by one manufacturer in 2024 claimed that it was less addictive than nicotin*e (148)*; however, others suggested that it is more potent in inducing analgesia and spontaneous motor activity *(149)*, indicating potent activation of nicotine receptors.

Vagg & Chapman *(150)* studied tobacco industry documents to identify industry activities with respect to nicotine analogues, including compounds such as 2'-methyltobacco and nicotine alkaloids such as anabasine and nornicotine *(143,150)*. They described industry exploitation of nicotine analogues in the 1970s and 1980s (mainly by R.J. Reynolds, Philip Morris International and British–American Tobacco). Initially, the industry became interested in nicotine analogues to circumvent any regulations on tobacco and nicotine, although they did not fully pursue their interest because they were concerned that it would lead to additional regulation of tobacco products. Other reasons for their interest in nicotine analogues were to further understand nicotine pharmacology (particularly to enhance its central effects while reducing peripheral effects), to assess pharmaceutical

applications (e.g. treating neurological disorders) and to evaluate the benefits for public relations of developing therapeutics. A key goal was to synthesize compounds that maintain or enhance the reinforcing properties of nicotine while reducing the negative side-effects (tachycardia, raised blood pressure) to create a less harmful and more desirable cigarette *(150)*. Although non-nicotine tobacco alkaloids such as anabasine, nornicotine, anatabine and myosmine are not well studied, addictive and reinforcing effects were observed in rats *(151–153)*.

Currently, there is no evidence of the use of nicotine analogues in commercial cigarette or cigarette-like products. Policy-makers should, however, consider the possibility of their use in cigarettes as a means of evading regulations on nicotine content, such as those proposed in New Zealand and the USA. An adaptation to preclude such concerns has been used in California, which will be effective in 2025, which extends the definition of nicotine to specify "any form of the chemical nicotine, including any salt or complex, regardless of whether the chemical is naturally or synthetically derived, and includes nicotinic alkaloids and nicotine analogs", while a tobacco product includes "a product containing, made, or derived from tobacco or nicotine that is intended for human consumption…" or "an electronic device that delivers nicotine or other vaporized liquids to the person inhaling from the device…." *(154)*.

6.4.4 Substitute fillers

Conventional tobacco cigarettes usually consist of a tobacco rod with chemical additives that are wrapped in paper or stuffed into a cigarette tube, which often also contains a filter. An emerging concern in the tobacco marketplace is introduction of substitute fillers to replace or supplement tobacco in products. For instance, in the context of a regulation to limit products containing tobacco material but not non-tobacco nicotine, rather than adding a tobacco rod to a cigarette, the rod could contain a different matrix or filler (such as tea leaves) infused with nicotine (or nicotine analogue). The idea of replacing tobacco in cigarette-like products is not novel. The idea had already been explored in the 1950s by the American Celanese Corporation (Cytrel) and in the 1960s by Imperial Tobacco (New Smoking Material) *(155)*. Substitute fillers were further investigated in the 1970s and 1980s in the United Kingdom in a "product modification programme", in which the Independent Scientific Committee on Smoking and Health was used as a bridge between the Government and the tobacco industry *(156)*. One goal of this programme was claimed to be to create a "safer cigarette" by substituting tobacco with other materials. In 1975, a new cigarette was issued, in which 25% of the tobacco was replaced by cellulose *(157)*. While these products gained substantial publicity *(155)*, their uptake by consumers was low *(158)*.

Another substitute filler may be herbs, and herbal cigarettes have appeared in various forms on the international market for decades. In China, the China

National Tobacco Company created herbal cigarettes in the 1970s that contained tobacco plant material, medicinal herbs and herbal extracts (e.g. ginseng) *(159)*. Other herbs used in herbal cigarettes have included damiana, mullein, coltsfoot, clove, lavender and peppermint, which may have various sensory, pharmacological and toxicological effects *(160)*. The first non-pharmaceutical herbal cigarette brand in China (such as for treating asthma and bronchitis *(161)*) was Changle, which was marketed by the Beijing Cigarette Factory in 1979; the brands proliferated in the 1990s as the products became more popular. Herbal cigarettes were then sold in Japan, the Republic of Korea, other South-East Asian countries and North America in the 2000s. Some international tobacco companies, such as Brown & Williamson and R.J. Reynolds, investigated Changle's herbal cigarettes but decided not to pursue them because of their potential toxicity and lack of sensory characteristics that were appealing for the US market *(161)*. One study in China indicated that being given tea cigarettes was associated with quitting failure *(162)*. Herbal cigarettes are also popular in India and elsewhere in South Asia in the form of traditional products such as *bidis*, which are thinly rolled cigarettes with crushed tobacco flakes wrapped in tobacco leaves that often contain herbs or spices; they are known to be harmful *(163,164)*. *Kreteks* are a type of cigarette that contains tobacco, cloves and other flavours that are popular in Indonesia *(165)*. Non-tobacco and non-nicotine herbal cigarettes have also emerged in the region, such as *maruk* and *maans nirdosh*, the latter of which is promoted as a herbal cigarette "believed to provide various health benefits, such as reducing stress and improving respiratory health" and is available in several variants of herbs and flavours *(161,166)*. No data are available, however, on the prevalence of use. "Hemp cigarettes" started to become available in 2020. One brand, TAAT, contains cannabidiol and a low level of delta-9-tetrahydrocannabinol but not nicotine and is promoted as an alternative to cigarette smoking *(167)*.

The levels of exposure to nicotine and other toxicants of people who smoke conventional cigarettes and those who smoke herbal cigarettes may be similar *(159)*, and a few studies have been reported on the health benefits of herbal cigarettes. The little available research shows they contain some toxicants at similar levels to those in conventional cigarettes (e.g. tar, carbon monoxide) *(168)* and may be equally harmful *(159,160)*. The addictiveness of these products has not been directly reported, but they are likely to have similar abuse liability, as the two types of product may contain similar levels of cotinine (i.e. nicotine) *(159)*. Companies nevertheless often market herbal cigarettes for their health benefits *(160,161,169,170)* and claim their benefit for cessation *(169,170)*. Herbal cigarettes are relatively popular among youth in India and the USA and are perceived as safer than tobacco cigarettes *(170,171)*. This indicates the importance of regulatory action on unsubstantiated claims for health and cessation in marketing *(159)*. Herbal cigarette makers could, however, adapt by promoting alternative flavours (as seen with menthol cigarettes in the USA) rather than making claims for health

or cessation *(161,172)*, indicating the importance of both regulatory action and a comprehensive ban on flavours.

The current EU Tobacco Products Directive *(173)* bans the use of characterizing flavours in heated tobacco products, which could prompt the industry to adopt non-tobacco based heatsticks (i.e. refill units for heating devices). These products are becoming available on global markets, particularly in the form of nicotine-infused herbal sticks intended for use with heated tobacco products *(174)*. For instance, British–American Tobacco has developed Veo sticks, which contain a nicotine-infused processed rooibos tea substrate in mint and fruit flavours. These products were launched in nine European countries in 2023, and British–American Tobacco planned to introduce them globally *(174,175)*. Philip Morris International introduced Levia in 2024, in which the sticks are made of nicotine-infused cellulose (a natural plant fibre), propylene glycol and flavourings. Levia has been found in Latin America, such as in Guatemala *(176)*. Because it contains no tobacco, Levia may allow Philip Morris International to avoid regulations and taxes in certain markets *(177)*. Imperial Brands have launched iSenzia sticks, which contain nicotine-infused oolong and green tea leaves *(174, 178)*. These herbal heat sticks are considered to have sales potential in eastern Europe because of their lower cost and national flavour preferences and also in Asia, where there is a history of herbal cigarette use *(174)*. Examples of similar products include Poda Holdings Inc. Beyond Burn Poda Pods *(179)*, which contain a

> tobacco-free blend of pelletized tea leaves infused with synthetic nicotine, which have been expertly crafted to mimic the sensorial experience of traditional cigarettes without the smoke, without the smell, and without the tobacco.

The company has noted that, as Beyond Burn Poda Pods do not contain tobacco, they are outside the scope of current tobacco regulation *(179)* and promotes the products as a reduced-risk replacement for conventional cigarettes *(180)*. The company ESON, in partnership with Poda for distribution in Europe and Asia *(181)*, has created the brand NEAFS, which are herbal sticks (herbs and tea leaves) infused with synthetic nicotine but no tobacco *(182)*. NEAFS sticks are intended to be used in the heating devices of heated tobacco products and are available in a variety of flavours *(182,183)*. The ingredients are described as "our premium cellulose blend, mint, edible essence, vegetable glycerin, and propylene glycol" *(183)*. The constituents of their cellulose blend and edible essence are not, however, described. Although these products are different from the tobacco sticks intended for use in heated-tobacco products, researchers and regulators must be vigilant for similar applications in conventional cigarettes. As of March 2025, no research had been published on these new product developments, and their potential appeal, addictive potential and toxicity are unknown. Such research would be complicated,

as a variety of substitutes can be used (e.g. different types of tea leaves), which may alter the appeal, addictive potential and toxicity of these products in various ways.

6.4.5 Filter (flavour) capsules

Another filter augmentation is a filter capsule containing a flavour liquid that is released into the filter once crushed. These capsules, which were first introduced in Japan in 2007 *(184)*, may contain menthol or other flavours (e.g. beverages, cocktails, fruit). Furthermore, some cigarette filters contain two flavour capsules with different flavours *(185)*. The identity of the flavour is not always clear from the product descriptors (e.g. Mega Ice Express, Tokyo Midnight, Ruby Fusion) *(186–188)*. Industry documents suggest that flavour capsule products were developed for youth and young adults who use cigarettes *(189,190)* to reduce their perceptions of harm and to increase appeal *(191)*. The filter capsules can be crushed by the consumer at any time during smoking, so that they can customize their smoking experience *(185,192)*. In addition, the filter capsule allows a larger concentration of flavouring to be transferred to the smoke, as the flavour liquid is not burnt with the tobacco *(192)*.

Brands with flavour capsules, including Marlboro, Pall Mall, Camel, Lucky Strike and Kent, are available globally *(184,185)*. Countries with a high prevalence of filter flavour capsule use include Argentina (17% in 2018), Chile (40% in 2018), Guatemala (33% in 2018), Japan (22% in 2021), Malaysia (27% in 2020), Mexico (50% in 2021), Peru (24% in 2018) and the Republic of Korea (32% in 2021), with a lower prevalence in Brazil (7% in 2016–2017) and in the USA (5% in 2014) *(185,187,188,193–196)*. Flavour capsule cigarettes first gaining popularity in the 2000s, and their the market share has grown substantially; as of 2025, it had surpassed that of non-capsule menthol cigarettes in many regions *(185,197)*. The marketing tactics (e.g. colour, technology, choice) of the tobacco industry are likely to increase sales of filter capsule cigarettes *(198)*.

6.5 Aftermarket modifiers of commercial cigarettes

Officials should also be aware of "aftermarket" products and accessories, such as filter capsules that can be inserted into a cigarette filter *(199,200)*. Advertisement videos for such accessories are shown on TikTok, primarily on the "TikTok shop" *(201)*. Many videos demonstrate addition of an aftermarket flavour capsule. A variety of flavours is available *(201)*. Inhalation of the contents of a capsule (e.g. menthofuran and pulegone) could be harmful *(202,203)*, and more and more countries are adopting more comprehensive regulatory measures on flavours to address the issue *(204–207)*. Certain countries have introduced measures to address accessories such as flavour capsules and synthetic coolants *(208)*.

Aftermarket products can be used with commercial cigarettes to alter their addictiveness, attractiveness or toxicity. Many such modifiers are increasingly

relevant and popular for future regulation (e.g. banning filters, limiting the nicotine content, removing flavourings) to limit changes to the design of commercial cigarettes at the point of manufacture.

6.5.1 Flavour cards or inserts

Havermans and colleagues in 2023 *(199)* found that aftermarket flavour accessories are widespread across the globe. The products include flavoured granules, threads, microcapsule coatings, heat-triggered capsules and filters that can be adjusted to alter smoke intensity, nicotine delivery and flavour *(203)*. They also include cards, filter tips and tubes for make-your-own cigarettes, drops, sprays, rolling papers, aroma markers, flavour stones and flavour powder *(199)*. For example, aftermarket flavour cards and other additives were found after the ban in Canada on menthol as a cigarette ingredient *(199)*. Aftermarket flavour capsules, cards and filter tips were the mode widely available and promoted; of 118 flavours available, menthol was that preferred *(199)*. Up to 9% of smokers in Netherlands (Kingdom of the) in 2021 had used such flavour accessories *(209)*.

6.5.2 Filter modifiers

Nicobloc (http://www.nicobloc.com/) is marketed by Nicobloc plc as a "stop smoking aid". It consists of water, corn syrup and citric acid. It is further claimed that, when applied to the filter, it reduces the amount of tar and nicotine emitted by up to 33% (two drops by 66%, three drops by 99%) according to the theory that the viscosity of the fluid will increase the efficacy of the filter to trap tar *(210)*. In 2022, this product was tested in a trial for smoking cessation in a community sample; however, no reduction in the number of cigarettes smoked per day was seen *(210)*. Gariti and colleagues tested a previous version of the product (AccuDrop) in a double-blind, placebo-controlled study with a combination of tapering cigarette smoking and brief counseling *(211)*. No significant difference was found in withdrawal scores between the groups, and the cotinine-validated abstinence rate at follow-up was similar in the two groups. In a laboratory study conducted in 1998, a similar solution (TakeOut) reduced nicotine levels when applied as directed, and subjects at the highest treatment condition (three drops, 45% lower nicotine boost) extracted 45% less nicotine *(212)*.

6.5.3 External filters

A number of aftermarket cigarette holders or filters (e.g. Zobo, BioPipe, NicoFree, TarTrap) are available that are marketed with the claim that they reduce the levels of toxicants in cigarettes smoke. No peer-reviewed study was found on the effectiveness of such filters in reducing toxicant emissions and/or the exposure of users. Zobo claimed that the filters contain "built-in microporous, beads and

fibers filter layers, helps catching the tar and stains". A number of versions are available, including for slim and superslim cigarettes, in different configurations and in both disposable and reusable versions. Cigarette holders were more common before widespread adoption of integrated cellulose acetate filters. A ban on filters integrated into the tobacco stick, particularly in a context in which many consumers believe that filters reduce harm, could increase the demand for such aftermarket external filter attachments. In 2021, about 4% of smokers in Netherlands (Kingdom of the) used such filters *(209)*.

6.5.4 Smoking devices

A recent product is the WONZ device, which can be described as a heating chamber for conventional cigarettes. As described by the manufacturer, a standard cigarette is placed in the device, which heats the tobacco material without setting it on fire and passes the aerosol across proprietary filters before reaching the mouthpiece. The filters are available in tobacco, menthol/mint, watermelon and tea flavours. In a trial with 50 cigarette smokers randomly assigned to smoke with or without the WONZ device (provided by the manufacturer), changes were measured in various biomarkers of exposure to smoke, health and subjective effects *(213)*. During 5 days of exclusive use, the level of exhaled carbon monoxide was about 70% lower, and reductions of 25–50% in smoke-associated biomarkers were observed in the group that used the device as compared with those who did not. During a subsequent 14-day trial, however, about half of users changed to dual use, with an overall increase in consumption, suggesting that the claims of reduced exposure may be tenuous. No studies were found on the attractiveness or addictiveness of WONZ. As heated tobacco products are introduced, consumers (and regulators) may confuse them with specifically designed consumables and a WONZ-type device that is used with conventional cigarettes, particularly in countries in which heated tobacco products and cigarettes are distinguished for tax or other regulatory reasons.

A number of "dry-herb vaporizers" are available on the market, usually associated with use of cannabis flower. Use of these vaporizers to heat tobacco has been addressed in only one study *(72)*, in which a vaporizer loaded with 1 g of roll-your-own cigarette tobacco was compared with the smokers' own brand of cigarette and an ENDS device by 15 participants in a laboratory study with fixed puffing patterns. The vaporizer increased the level of plasma nicotine to a lesser extent than the smokers' own brand (14.3 ng/mL vs 24.4 ng/mL), and the level was equivalent to that of the tested e-cigarette, with no substantial exposure to carbon monoxide. No other biomarkers were reported. No studies of actual use or of the addictiveness or attractiveness of such products were found. Such products could, however, be marketed to cigarette smokers in response to regulatory changes such as filter bans, nicotine content limits or flavour bans.

6.6 Discussion

In the past, the tobacco industry identified and used loopholes to circumvent regulations (e.g. a ban on non-menthol flavoured cigarettes resulted in marketing of flavoured cigarillos). There is no reason to believe that such behaviour will not continue, particularly as marketing and promotion become constricted and overall prevalence of tobacco use decreases. Coherent, integrated, systemic understanding of the dynamic relations among policies, cigarette design and smokers' perceptions, behaviour and exposure requires rigorous, independent scientific research. WHO Member States should determine the optimal policies and regulations for these products to protect national and global public health. WHO TobReg plays a crucial advisory role by summarizing current scientific findings and making evidence-based recommendations for policy in the context of the evolving marketplace.

A rapid surveillance system could be used to inform Member States about developments in the cigarette (and adjacent product) marketplace. This has been attempted on several occasions *(3,214–216)* but is difficult to maintain without dedicated funding. Furthermore, separating product "fads" from products with a more significant impact can be difficult. In 2023, the US FDA funded the Center for Rapid Surveillance of Tobacco (CRST; https://tobaccocrst.org/about-us), to collect data on the sales, marketing and use of new and modified products. A network of sentinel sites across the country generates data on new and emerging products to identify those most likely to be taken up (e.g. rapidly increasing sales, extensive promotion or visibility). CRST does not, however, monitor product characteristics or features, although this could be done independently and integrated. The National Institute for Public Health and the Environment in Netherlands (Kingdom of the) monitors products reported under the European Tobacco Products Directive *(217)*, including content, emissions, marketing, health risk assessment and investigations into use and product perceptions. Such rapid surveillance and monitoring systems could be used as models for other jurisdictions for developing rapid surveillance programmes, particularly to link surveillance data to mandated company disclosures on product features that could increase uptake. Such a system could foster forecasting models that integrate data streams and provide predictions.

WHO Member States and Parties to the WHO FCTC should address cigarette-related regulations comprehensively to ensure that new designs do not gain a foothold as the sales of conventional cigarettes and the prevalence of smoking decrease. Broad regulations allow enforcement authorities to adapt to many future product changes without requiring authority from legislative or other bodies *(133)*. Member States should support independent scientific research on the toxicity, addictiveness and appeal of these products. Governments must evaluate their definitions of cigarettes and ensure inclusion of the definitions of potential replacement or augmentation products that are subject to and not subject to their

regulations. For example, Member States that have specific nicotine regulations (e.g. maximum nicotine limits, regulation of tobacco-derived nicotine) should avoid leaving loopholes that could be circumvented by the tobacco industry with analogues, synthetics and minor tobacco alkaloids. In some states and localities in the USA, regulatory loopholes on little cigars were closed by establishing tax parity with cigarettes and restrictions on packaging of and flavourings in these products *(114)*. Regulators should anticipate future developments and address nicotine analogues, synthetics, tobacco alkaloids and other alterations that are being used or likely to emerge (e.g. with similar chemical structures or similar biological activity) *(136,150)*. Similarly, consistent with WHO FCTC Article 10, regulators must require that manufacturers declare all ingredients and additives in cigarettes and should introduce standardized labelling to ensure that such chemicals are not included in cigarettes or will be explicitly declared. The WHO FCTC includes "products entirely or partly made of the leaf of tobacco as raw material" in the definition of "tobacco products" *(218)*, which may not cover analogues or alternative fillers. WHO Member States should therefore explicitly address these alternatives. The Conference of the Parties in 2023 requested the Secretariat of the WHO FCTC to consider a classification of new and emerging nicotine and tobacco products *(219)*. Regulations that address only tobacco plant material or tobacco-derived nicotine do not comprehensively cover contemporary products, and the tobacco industry is actively adapting product lines to circumvent existing regulations, which are relevant for the tobacco market that was prevalent at the time the WHO FCTC was adopted. Standard definitions and naming conventions for new products will be an important first step.

6.7 Recommendations

6.7.1 Short-term

- Restrict the use of synthetic nicotine and nicotine analogues, as these and non-tobacco substitute fillers are a foreseeable mechanism by which regulations on the upper limits of cigarette nicotine content could be circumvented. Regulators could consider disallowing their use a priori without evaluation or authorization from a competent regulatory body.
- Develop methods and infrastructure for surveillance and forecasting to provide better information for regulators about developments in the market. Surveillance could cover several data streams (e.g. industry disclosures, sales data, product contents and emissions) to provide information on distinctive features of emerging products or product modifications in response to regulations.
- Consider more inclusive regulations (such as banning all compounds

that bind to the TRPM-8 receptor). Synthetic coolants are being used to circumvent characterizing flavour bans and particularly menthol. A "white list" approach could be considered, in which additives that are not on a list of permissible additives are presumptively banned. Such an approach could slow the proliferation of replacement additives and, importantly, shift the burden of proof that a product is in compliance to the manufacturer.

6.7.2 Medium- and long-term

- Fund industry-independent research on emerging products to better understand their chemistry, toxicology, safety and abuse liability to provide information on how emerging product designs might best be regulated.
- Develop and/or validate standardized, non-targeted methods for identifying tobacco product additives of potential concern. Such methods might be developed under the auspices of TobLabNet.
- Move towards regulatory standardization of tobacco products to remove differences among products that disproportionally influence their attractiveness, addictiveness or toxicity. For example, remove filters or mandate a standard diameter and length.

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7. Aldehydes and metals in e-liquids as potential targets for regulation

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Contents

Abstract
7.1 Background
7.2 Methods
7.3 Overview of e-liquid composition
7.3.1 Toxicants in e-liquids
7.4 Aldehydes in e-liquids
7.4.1 Types and content of aldehydes in e-liquids
7.4.2 Characteristics of aldehydes in e-liquids
7.4.3 Determination of aldehydes in e-liquids
7.4.4 Implications of the presence of aldehydes in e-liquids
7.4.4.1 Attractiveness
7.4.4.2 Addictiveness
7.4.4.3 Possible effects on toxicants in e-cigarette aerosol
7.5 Metals in e-liquids
7.5.1 Types and content of metals in e-liquids
7.5.1.1 Factors associated with higher metal concentrations in e-liquids
7.5.1.2 Transfer of metals from e-liquids to aerosols
7.5.2 Characteristics of metals in e-liquids
7.5.3 Determination of metals in e-liquids
7.5.4 Toxicity implications of the presence of metals in e-liquids
7.5.4.1 Exposure of e-cigarette users to metals
7.5.4.2 Toxic and carcinogenic effects of metals in e-cigarettes
7.6 Regulation of aldehydes and metals in nicotine and tobacco products
7.7 Summary and conclusions
7.8 Research directions
7.9 Policy recommendations
References

Abstract

E-liquid content is a major contributing factor to the chemical profile of e-cigarette aerosols. Regulation of e-liquid contents could minimize the potential for the short- and long-term toxicity of e-cigarette use. Aldehydes (often from flavours or as decomposition products) and metals (that leach from the device itself) are frequently reported as non-primary ingredients or contaminants in e-liquids (i.e. excluding nicotine and the aerosol-forming solvents propylene glycol and glycerine) and are potential sources of toxic or carcinogenic components of e-cigarette

aerosol. This paper reviews the literature on the presence and pathways of these compounds during e-cigarette use. Commonly occurring aldehydes in e-liquids are formaldehyde, acetaldehyde, benzaldehyde, vanillin and ethyl vanillin; other aldehydes such as citral and cinnamaldehyde are also routinely detected in e-liquids. Formaldehyde and acetaldehyde, which are established carcinogens, are among the decomposition products formed during heating of major e-liquid constituents. Other aldehydes have flavour properties and are added to e-liquids to enhance their attractiveness. The flavouring aldehydes are generally recognized as safe when consumed as components of food, but their toxicity as constituents of e-cigarette aerosol is unknown. In addition to aldehydes, many metals, including carcinogens such as arsenic, cadmium, chromium VI, lead and nickel, have been detected in e-liquids and aerosols. Their potential sources including contamination from the metal parts of e-cigarette devices, including coils. There is evidence that metals in e-liquids are transferred to the aerosol. We discuss directions for future research and provide recommendations for regulating aldehydes and metals in e-liquids.

Keywords: Electronic cigarettes, e-liquids, aldehydes, flavours, metals, attractiveness, addictiveness, toxicity

7.1 Background

This report addresses aldehydes and metals in electronic cigarette liquids (e-liquids). The accumulating published data indicate that certain e-liquids and e-cigarette aerosols contain substantial levels of harmful agents, raising concern about their potential toxicity in users. As some of these harmful agents can be transferred directly from e-liquids, their removal could minimize the toxicity of e-cigarette aerosols. They include aldehydes, which are often present in flavourings for e-liquids, and metals, which are probably introduced as contaminants or leach into the liquids from various components of e-cigarette devices. While e-cigarettes expose users to fewer chemicals than cigarettes and other conventional tobacco products, and biomarker data show decreased exposure to many toxicants and carcinogens, limited evidence is available on the long-term effects of e-cigarette use. E-cigarettes are highly heterogeneous, and users of these products often do not know what they are inhaling. For example, they are recently being used increasingly to administer drugs such as etomidate, with many users not being aware of its presence of in the products.

The partial guidelines for implementation of Articles 9 and 10 of the WHO FCTC *(1)* provide Parties with an outline for regulating tobacco products and using disclosures as a tobacco control measure. Such measures may include standards on product composition, such as setting limits on certain constituents in product contents and emissions and/or prohibiting certain additives. Product standards can have a direct impact on reducing the addictiveness, attractiveness and toxicity of

tobacco and nicotine products and, as a consequence, on decreasing the morbidity and mortality attributable to their use. As e-liquid content is a major contributor to the chemical profile of e-cigarette aerosols, their regulation is an important, straightforward initial step towards minimizing the potential short- and long-term toxicity of e-cigarette use. Aldehydes are added to liquids as flavouring agents, and both aldehydes and metals are known to have potential toxic and carcinogenic effects, as discussed below. Therefore, regulation of these constituents in e-liquids may be an appropriate measure for protecting public health.

This paper provides an overview of the current state of knowledge on aldehydes and metals in e-cigarette liquids, including their levels and methods for their measurement, as well as implications for product attractiveness, addictiveness and toxicity. Examples of country experience in regulating these constituents and other relevant product standards are summarized. Finally, we identify research gaps and priorities and provide policy recommendations. Specifically, this paper covers the following:

- an overview of e-liquid composition, including toxicants and types of nicotine;
- types and levels of aldehydes found in e-liquids and implications for product attractiveness, addictiveness and toxicity;
- types and levels of metals found in e-liquids and implications for product attractiveness, addictiveness and toxicity;
- regulatory considerations and country experiences;
- summary and conclusions;
- research gaps and priorities; and
- policy recommendations.

7.2 Methods

The literature was searched between January and November 2024, primarily on the PubMed database. Relevant articles cited in publications obtained through the database search were also included. The search was conducted with the terms "e-cigarette aldehydes" and "e-cigarette liquids metals", with no limit on the date of publication. Abstracts were inspected for relevance to the topic, and the relevant publications were collected for this review. We also reviewed the websites of various regulatory agencies and other information relevant to country experience in regulation of constituents.

7.3 Overview of e-liquid composition

E-cigarettes and e-liquids have been evolving since their first introduction onto global markets in 2003. Currently, a wide variety of devices and e-liquids is

available worldwide, contributing to the chemical variability of product emissions and user exposures.

The composition of e-liquids is complex. The primary ingredients commonly present in various e-liquid brands and types include a combination of propylene glycol and glycerine (the solvent), nicotine and nicotine modifiers (organic acids, nicotine salt-based products) and flavouring additives. In addition, e-liquids contain a number of contaminants, which are either introduced during e-liquid manufacture, leached into e-liquid during product storage and/or use or formed as a result of e-liquid ingredient decomposition (e.g. thermal, ageing).

7.3.1 Toxicants in e-liquids

Toxicants and carcinogens found in e-cigarette liquids include tobacco alkaloids, amides, aromatic amines, metals, tobacco-specific *N*-nitrosamines, phenols, various aldehydes, esters, alcohols, ketones and flavouring-related constituents *(2–5)*. In a recent publication, researchers at the Center for Tobacco Products of the US Food and Drug Administration concluded that 36 of the 93 harmful and potentially harmful constituents are present in e-liquids at quantifiable levels, and they categorized them according to their sources (Table 7.1) *(4)*. This framework can be used for categorizing, monitoring, and regulating all harmful constituents in e-liquids.

Table 7.1. Sources of toxicants and carcinogens in e-liquids

Source	Examples of harmful constituents	References
Added ingredients	Nicotine	*(6,7)*
Impurities from e-liquid formulation or plastic device components and parts	Anabasine, nornicotine, tobacco-specific nitrosamines, benzene, ethylbenzene, styrene, toluene	*(6–9)*
Impurities or other contaminants from e-liquid manufacture or storage	Polycyclic aromatic hydrocarbons	*(10,11)*
A combination of sources, such as an impurity, a flavourant or degradant or an environmental contaminant	Phenols, acrylamide, o-toluidine, aldehydes and other carbonyls, metals and metalloids	*(7,10–12)*

Source: Adapted from Reilly et al. *(4)*

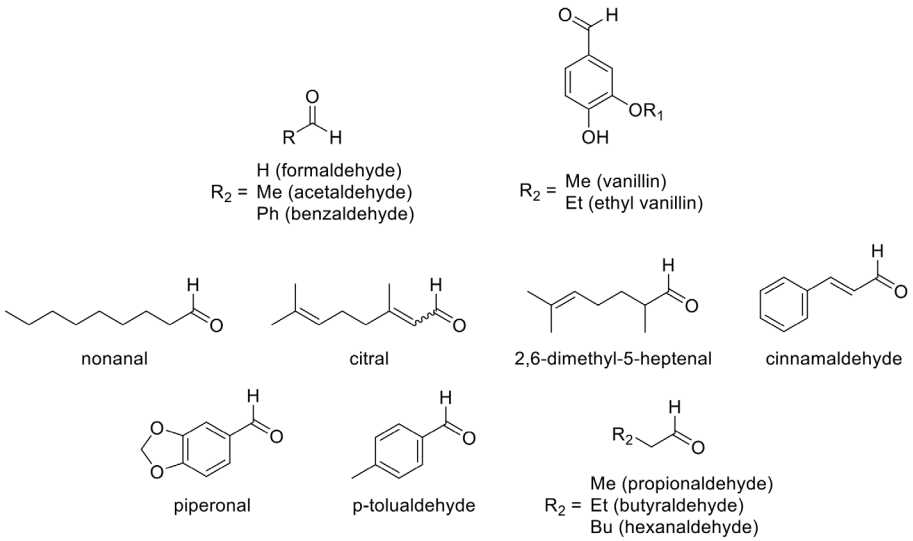
While a recent umbrella review of the chemical profiles of e-cigarettes highlighted the significant heterogeneity in the reported levels of such harmful agents in different studies (probably due to the heterogeneity of products), studies consistently show the presence of these constituents in various products *(2)*. Similarly, while the mechanisms of the toxicity of flavouring additives are not yet fully characterized, studies in experimental models (e.g. in vitro and in vivo) suggest that flavoured e-liquids are toxic, the outcomes including cell necrosis, altered cell morphology, oxidative stress, inflammatory processes and other biological effects relevant to the pathology of various chronic diseases; however, further research is required *(4,13,14)*.

7.4 Aldehydes in e-liquids

7.4.1 Types and content of aldehydes in e-liquids

A review by Eshraghian and Al-Delaimy *(5)* listed the aldehydes found in many different e-liquids. To be listed, an aldehyde was required to have been present in 50% of samples of a given e-liquid in at least one study. Accordingly, the following aldehydes were listed as components of e-liquids: formaldehyde, acetaldehyde, benzaldehyde, vanillin and ethyl vanillin. The frequency of occurrence of each aldehyde in samples of each listed e-liquid was also reported. For example, acetaldehyde occurred in 10 of 21 samples analysed in one study and in 42 of 42 in another. In studies not included in the review, some additional aldehydes were reported to occur commonly: nonanal, 3,7-dimethyl-2,6-octadienal (citral), 2,6-dimethyl-5-heptenal, cinnamaldehyde, piperonal *(15–17)*, *p*-tolualdehyde *(18)*, hexanaldehyde *(19)*, propionaldehyde and butyraldehyde *(11)*. The structures of these compounds are shown in Fig. 7.1. In a comprehensive study of flavourings in e-liquids sold in Netherlands (Kingdom of the), vanillin, ethyl vanillin and benzaldehyde were most frequently used *(20)*.

Fig. 7.1. Structures of aldehydes found commonly in e-liquids



7.4.2 Characteristics of aldehydes in e-liquids

While volatile aldehydes such as formaldehyde and acetaldehyde are produced during heating of the major components of e-liquids, propylene glycol and glycerine, higher-molecular-weight aldehydes are probably added to e-liquids because of their flavouring properties. Some relevant characteristics of aldehydes in e-liquids are presented in Table 7.2.

Table 7.2. Some fundamental characteristics of aldehydes in e-liquids

Compound	Melting-point (°C)	Boiling-point (°C)	Relevant properties
Formaldehyde	–92	–19	Pungent colourless gas that polymerizes readily
Acetaldehyde	–123.37	20.2	Colourless liquid with a green apple flavour
Propionaldehyde	–81	46–50	Colourless liquid with a pungent fruity and floral odour
Butyraldehyde	–96.86	74.8	Colourless liquid with cocoa and green flavour profile
Hexanaldehyde	≤ 20	130–131	Liquid used to produce fruity, green flavours
Nonanal	–18	191	Colourless oily liquid with a citrus-like rose-like odour
2,6-Dimethyl-5-heptenal	Not available	116–124/100 mL	Liquid with fruit, green, melon flavour
3,7-Dimethyl-2,6-octadienal (citral)	≤ 10	229	Pale yellow lemon-scented liquid
3-Phenylpropenal (cinnamaldehyde)	–7.5	248	Gives cinnamon its flavour and odour
3,4-Methylenedioxy)benzaldehyde (piperonal)	37	263	Has a floral odour similar to vanillin or cherry
Benzaldehyde	–57.12	178.1	Has an almond-like odour
p-Tolualdehyde	–6.00	204–205	Has a cherry-like odour
3-Methoxy-4-hydroxybenzaldehyde (vanillin)	81	285	Principal flavour and aroma compound in vanilla
3-Ethoxy-4-hydroxybenzaldehyde (ethyl vanillin)	76	295.1	More potent than vanillin as a flavour agent

Melting-point and boiling-point are characteristics relevant for the chemical compound's capacity for aerosolization.
Source: Kim et al. *(21)*

Selected data on toxicology and carcinogenicity

Most of the data reported here, with the exception of those for acetaldehyde and formaldehyde, are from studies in which exposure was not by inhalation, which are the most relevant to the potential toxic and carcinogenic effects of e-cigarette use. Furthermore, while the available studies provide valuable insights, the quality of each study has not been rigorously evaluated.

Formaldehyde. An international group of experts assembled by the International Agency for Research on Cancer concluded that there was sufficient evidence in humans for the carcinogenicity of formaldehyde and that it causes cancer of the nasopharynx and leukaemia *(22)*. The American Cancer Society summarized evaluations of the carcinogenicity of formaldehyde by the National Toxicology Program (NTP) and the Environmental Protection Agency in the USA *(23)*. The latter listed formaldehyde as "known to be a human carcinogen" and classified formaldehyde as "carcinogenic to humans by the inhalation route of exposure", with increased risks of nasopharyngeal cancer, nasal sinus cancer and myeloid leukaemia and evidence suggesting increased risks for some other types of cancer.

Acetaldehyde. Acetaldehyde is the main metabolite of ethanol. The results of studies of individuals with genetic polymorphisms that increase blood or salivary levels of acetaldehyde after alcohol consumption show dose–response relations between alcohol consumption and cancers of the oral cavity, pharynx, larynx and oesophagus and possibly of the stomach and colorectum. A working group at the International Agency for Research on Cancer (IARC) concluded that the association of acetaldehyde with alcohol consumption is carcinogenic to humans *(24)*. The NTP stated that acetaldehyde is reasonably anticipated to be a human carcinogen *(25)*.

Propionaldehyde. Propionaldehyde has been approved by both the US FDA *(26)* and the Joint Food and Agriculture Organization of the United Nations and WHO Expert Committee on Food Additives *(27)* as a synthetic flavouring ingredient for direct addition to food. Male and female rats were exposed by inhalation to 90 ppm propionaldehyde 6 h/day for 20 exposures or to 1300 ppm 6 h/day for 6 days. No changes in body weight or clinical signs were observed. Microscopic examination revealed liver cell vacuolation in animals exposed to 1300 ppm propionaldehyde.

The genotoxicity of propionaldehyde has been studied in bacteria and in mammalian cells in vitro. Mixed results were obtained in different systems. It was mutagenic in *Salmonella typhimurium* strain TA1534 but inactive in other strains. It induced chromosome aberrations in Chinese hamster embryonic cells and chromosome breaks in Chinese hamster ovary cells and induced a concentration-related increase in unscheduled DNA synthesis in rat hepatocytes but had no effects on human hepatocytes *(28)*.

Butyraldehyde. Butyraldehyde was less toxic than acetaldehyde and propionaldehyde in various animal species. High aerosol concentrations (197–230 ppm) cause irritation to the eyes, nose and throat of humans. The results of genotoxicity studies were generally negative. Data on acute median lethal dose (LD_{50}) indicate low toxicity by the oral, dermal and inhalation routes of exposure. The results of studies of genotoxicity in four in-vitro assays were negative *(29)*.

Hexanaldehyde. In a short-term oral toxicity study, groups of 10 male and 10 female rats were given drinking-water containing a concentration of 1, 10, 100 or 1000 mg/L hexanaldeyde for 4 weeks. No significant toxic effects were observed. Exposure of female mice to 1000 mg/kg, however, caused a significant increase in tubular cytoplasmic inclusions in the kidney over that in controls *(30)*.

Nonanal. Nonanal did not induce unscheduled DNA synthesis in adult human hepatocytes at 3–100 mM. It induced sister chromatid exchange in rat hepatocytes at 0.1–100 μM but not unscheduled DNA synthesis in adult rat hepatocytes at 3–100 mM. It induced forward mutations in V79 Chinese hamster lung cells at 0.1–0.3 mM but was not genotoxic in a modified Ames test (preincubation method) in *S. typhmiurium* TA98, TA100 or TA1535 at 1–666 μg/

plate. It also gave negative results in an Ames test with *S. typhmiurium* TA102 and TA104 at up to 1 mg/plate and in a chromosomal aberration test in rat hepatocytes at 0.4 µg/mL *(31)*.

2,6-Dimethyl-5-heptenal. 2,6-Dimethyl-5-heptenal was not mutagenic in an Ames test in *S. typhimurium* strains TA 98, 100, 1535 or 1537 at doses up to 50 mg/plate and did not induce unscheduled DNA synthesis in rat hepatocytes at 1 mg/mL *(32)* or micronucleus formation in mice at up to 1540 mg/kg bw *(33)*. In groups of 15 male and 15 female rats fed diets providing 2,6-dimethyl-5-heptenal at an average intake of 0, 9, 37 or 150 mg/kg bw per day for at least 90 days, histological examination of rats at the high dose showed no statistically significant difference from controls, other than alveolar thickening in males ($P < 0.05$). The no-observed-effect level of 2,6-dimethyl-5-heptenal was 37 mg/kg bw per day *(34)*.

3,7-Dimethyl-2,6-octadienal (citral). Citral gave negative results in several genotoxicity assays. In male Wistar rats and male LACA mice, citral was rapidly absorbed from the gastrointestinal tract and distributed throughout the body, independent of the dose administered. In both species, the radiolabel was excreted rapidly, most being excreted within 24 h, predominantly in the urine but also in exhaled air (as $^{14}CO_2$) and faeces. The NTP tested citral for carcinogenicity *(35)* and concluded that "under the conditions of this 2-year feed study there was no evidence of carcinogenic activity of citral in male or female F344/N rats exposed to 1000, 2000, or 4000 ppm". The no-observed-adverse-effect level for citral was 100 mg/kg bw per day on the basis of decreased body weights (in particular in females) *(36)*.

3-Phenylpropenal (cinnamaldehyde). Cinnamaldehyde was enclosed in starch microcapsules and added to the feed of rats and mice for 2 years at a dose of 1000, 2100 or 4100 ppm. Control animals received empty starch microcapsules. Tissues from more than 40 sites were examined for each animal. Rats that received 4100 ppm cinnamaldehyde and mice that received 2100 or 4100 ppm weighed less than controls, although they ate the same amount of feed. No tumours or other toxic effects were observed in either of the species given cinnamaldehyde *(37)*. Cinnamaldehyde is frequently found at a relatively high concentration (10 mM) in flavoured e-cigarette liquids *(38)*. It temporarily suppressed ciliary motility in human bronchial epithelial cells by dysregulation of mitochondrial function *(39)*.

(3,4-Methylenedioxy)benzaldehyde (piperonal). In male rats, piperonal administered in propylene glycol by gavage was accounted for in urine within 24 h. No unchanged compound was excreted. The main urinary metabolite was piperonylic acid and its glycine conjugate. No metabolites were detected in urine more than 48 h after dosing. An LD_{50} of 2700 mg/kg body weight of piperonal administered by gavage was reported in rats. Piperonal was not mutagenic in many tests in *S. typhimurium* strains *(40)*.

Benzaldehyde. Benzaldehyde is generally regarded as safe as a food additive in the USA and is accepted as a flavouring substance in the EU. It does

not accumulate in any tissue type and is metabolized to benzoic acid and its conjugates, which are excreted in the urine. The oral LD_{50} of benzaldehyde in rats and mice ranged from 800 to 2850 mg/kg. Repeated inhalation of volatilized benzaldehyde produced ocular and nasal irritation at 500 ppm and death in rabbits at 750 ppm. Benzaldehyde was not mutagenic in bacterial assays but induced chromosomal abnormalities in Chinese hamster cells and increased mutations in a mouse lymphoma forward mutation assay. The NTP found no evidence of carcinogenicity in rats but some evidence of carcinogenicity in mice *(41)*.

p-Tolualdehyde. *p*-Tolualdehyde was administered to 10 rats (sex and strain not indicated) at a dosage range of 200–3200 mg/kg. No unusual clinical signs were observed, except for evidence of slight toxicity. The LD_{50} was 1600 mg/kg. *p*-Tolualdehyde was administered by gavage to groups of five rats (sex and strain not indicated) at 100 or 1000 mg/kg per day for a total of 12 doses over 17 days. Feed consumption and weight gain were normal. Haematology, clinical chemistry, liver and kidney weights and gross and histopathological findings were normal *(42)*.

3-Methoxy-4-hydroxybenzaldehyde (vanillin). Vanillin injected intraperitoneally into strain A mice at total doses of 3.6–18.0 g/kg over 24 weeks caused no excess number of lung tumours and was considered not to be carcinogenic. Groups of 16 rats fed diets containing vanillin at levels that provided 20 mg/kg body weight per day for 18 weeks had no adverse effects, but a dose of 64 mg/kg/day for 10 weeks depressed growth and damaged the myocardium, liver, kidney, lung, spleen and stomach *(43)*.

3-Ethoxy-4-hydroxybenzaldehyde (ethyl vanillin). Groups of 12 male and 12 female rats were fed diets containing 0, 0.5, 1 or 2% ethyl vanillin for 2 years or 2% or 5% for 1 year with no adverse effect on growth, weights of major organs, haematology or the histology of major tissues. In genotoxicity studies, ethyl vanillin did not induce genetic changes in vitro but was reported to increase the ability of mitomycin C to cause sister chromatid exchanges *(44)*.

In summary, with the exception of formaldehyde and acetaldehyde, the aldehydes listed here do not appear to present concern about toxicity, including genotoxicity, when considered as components of e-liquids. Their transfer to aerosols or possible decomposition to other products upon heating could, however, raise issues, as discussed below.

7.4.3 Determination of aldehydes in e-liquids

The methods used for determination of aldehydes in e-liquids are summarized in Table 7.3. The aldehydes were analysed either directly by gas chromatography–mass spectrometry (GC-MS) if sufficiently volatile or as their 2,4-dinitrophenylhydrazone (2,4-DNP) derivatives, which are readily formed in high yields and are analysed either by liquid chromatography (LC) with detection by ultraviolet absorbance (UV) or by LC-MS.

Table 7.3. Methods used for the determination of aldehydes in e-liquids

Aldehyde	Method	Reported concentration	Reference
Formaldehyde	2,4-DNPs by LC-UV or LC-MS	0.114–9.00 µg/g	*(19)*
Acetaldehyde	Headspace GC-MS	0.050–10.2 µg/g	*(19,45)*
Propionaldehyde	2,4-DNPs by LC-UV or LC-MS	<0.043–0.261 µg/g	*(19)*
Butyraldehyde	2,4-DNPs by LC-UV or LC-MS	<0.077–1.03 µg/g	*(19)*
Hexanaldehyde	2,4-DNPs by LC-UV or LC-MS	<0.036–0.532 µg/g	*(19)*
Nonanal	GC-MS	Not reported	*(16)*
2,6-Dimethyl-5-heptenal	GC-MS	Not reported	*(16)*
Citral	GC-MS	Not reported	*(16)*
Cinnamaldehyde	GC-MS	< 2.2–140,000 µg/mL	*(46)*
Piperonal	GC-MS	Not given	*(15)*
Benzaldehyde	2,4-DNPs by LC-UV or LC-MS	46.8–98.5 µg/mL	*(15,19)*
p-Tolualdehyde	2,4-DNPs by LC-UV or LC-MS	< 0.018 µg/g	*(19)*
Vanillin	GC-MS	277.1–5365 µg/mL	*(15)*
Ethyl vanillin	GC-MS	289.5–2447 µg/mL	*(15)*

7.4.4 Implications of the presence of aldehydes in e-liquids

7.4.4.1 Attractiveness

With the exception of formaldehyde, which is probably an impurity introduced during the manufacture of e-liquids or generated as decomposition product, all the compounds discussed here have flavour attributes, as noted in Table 7.2, and are added to e-liquids to increase their attractiveness. All the compounds, with the exception of formaldehyde, are "generally recognized as safe under their conditions of intended use as flavouring ingredients added to human food", according to evaluations by the Flavor and Extract Manufacturers Association Expert Panel *(47)*. It is not known whether a statement similar to "generally recognized as safe" would apply to use of these compounds in e-liquids.

7.4.4.2 Addictiveness

Formaldehyde and acetaldehyde might increase the addictiveness of nicotine *(48)*, possibly affecting the extent of e-cigarette use. None of the other substances listed here have established addictive properties themselves.

7.4.4.3 Possible effects on toxicants in e-cigarette aerosol

These compounds can be transferred to e-cigarette aerosol, depending on the e-liquid composition and the device operating temperature. Formaldehyde, acetaldehyde and acrolein are routinely detected in e-cigarette aerosol as decomposition products of propylene glycol and glycerol. Other aldehydes detected in e-cigarette aerosol are methyl glyoxal, propionaldehyde, butyraldehyde, isobutyraldehyde, crotonaldehyde, hexanaldehyde, benzaldehyde, *p*-tolualdehyde

and vanillin *(5,49,50)*. Pyrolysis of aldehydes to release carbon monoxide and alkyl fragments generally requires higher temperatures than those reached during use of e-cigarettes *(51)*. Aldehydes in e-liquids can react with propylene glycol and glycerol to produce adducts that have not been fully evaluated for their effects on e-cigarette aerosols *(52,53)*.

7.5 Metals in e-liquids

In this paper, the term "metals" includes various elements that are classified as metals and metalloids and are referred to in the literature on e-cigarettes as metals, heavy metals and metalloids. Metals are defined chemically as "elements which conduct electricity, have a metallic luster, are malleable and ductile, form cations, and have basic oxides" (e.g. nickel [Ni], cobalt [Co] and cadmium [Cd]), while metalloids are elements with the appearance of metals but with different chemical properties (e.g. arsenic [As] and antimony [Sb]), although the classification of elements as metalloids is not consistent. While the term "heavy metals" is commonly used by some researchers and regulators, there is no single, generally agreed upon list of elements classified as such. Indeed, according to a technical report by the International Union for Pure and Applied Chemistry, there is no chemical or toxicological basis for this classification and "there is no authoritative definition" *(54)*.

The presence of at least 35 metals in e-cigarette liquids and aerosols has been reported by various researchers and summarized in several systematic reviews *(2)*. Metals may originate from the parts of the device, including coils and soldered joints of coils and may also be present as contaminants in e-liquids *(55–59)*.

7.5.1 Types and content of metals in e-liquids

The composition of coils and soldering are major determinants of the types of metals found in e-liquids exposed to these parts of the e-cigarette device *(60)*. For example, commonly used coils may be made of single metals (e.g. Ni) or alloys (e.g. kanthal, which contains Al, iron (Fe) and chromium (Cr) or nichrome, which contains Ni and Cr, while soldered joints contain tin (Sn), Sb and potentially other metals *(56–59,61)*. It has also been reported that soldered joints of poor quality or with signs of fraying are associated with higher levels of Sn in e-liquids *(61,62)*. Contaminants in e-liquids originating from ingredients and reagents used in e-liquid preparation may include Cd, As, lead (Pb), silicon and other metals *(56–59)*. This may also arise from components used in the device.

Table 7.4 summarizes the ranges of levels of some metals reported to be present in e-cigarette liquids. The number of metals analysed differed by study, and there is substantial variation in the metals measured by brand, e-liquid and device type, as well as over time (as the design evolved) *(2)*. The levels of metal

in e-liquids that are sold in bottles are usually lower than those in cartridges or tanks, which is likely to be due to lack of contact with the device components. The liquids do, however, become contaminated after they are placed in the device and during product use *(2)*. Conditions and device characteristics that contribute to higher levels of metals in e-liquids and to their transfer from e-liquids to aerosols are summarized in subsequent sections.

Table 7.4. Potential sources and levels of some metals in e-liquids

Element	Classification	Reported harmful effects	Possible source(s) in e-liquid	Levels reported, ng/mL	References
Aluminium (Al)	Metal	Respiratory toxicity, neurotoxicity	Coil, other parts of heating elements (wicks, sheaths, joints)	6.6–101	*(10,57,59,63)*
Arsenic (As)	Metalloid	Carcinogen (lung, liver, bladder), neurotoxicant, respiratory toxicant	Contamination in e-liquid ingredients, leaches from e-liquid container materials	0.07 –4.2	*(10,57,59,63–65)*
Cadmium (Cd)	Transition metal	Lung carcinogen, respiratory toxicant, probably developmental toxicity	Contamination in e-liquid ingredients, leaches from e-liquid container materials	< 0.009 (LOD) –176	*(10,57,59,63,65–67)*
Cobalt (Co)	Transition metal	Neurotoxicity, cardiovascular toxicity, potential respiratory toxicity	Contamination in e-liquid ingredients, leaches from e-liquid container materials	0.1 –10.8	*(10,57,59)*
Chromium (Cr)	Transition metal	Cr VI: respiratory toxicant, carcinogen	Coil, other parts of heating elements (wicks, sheaths, joints), contaminant in e-liquid ingredients, leaches from e-liquid container materials	1.6–1815[a]	*(10,57,59,64,67)*
Copper (Cu)	Metal	Respiratory irritation and toxicity	Parts of heating elements (wicks, sheaths, joints)	< 0.009 (LOD) –176	*(10,57,59,63)*
Iron (Fe)	Transition metal	Cardiovascular toxicity, neurotoxicity, carcinogenesis	Coil, other parts of heating elements (wicks, sheaths, joints)	3.5 –1880	*(57,63)*
Manganese (Mn)	Metal	Neurotoxicity, respiratory toxicity	Coil, other parts of heating elements (wicks, sheaths, joints)	0.1–5943	*(10,57,59,63,67)*
Nickel (Ni)	Transition metal	Respiratory irritant and toxicant, lung and nasal carcinogen	Coil, other parts of heating elements (wicks, sheaths, joints)	0.1 –19 436[a]	*(10,57,59,63–67)*
Lead (Pb)	Metal	Neurotoxicity, carcinogenicity	Contamination in e-liquid, leaches from e-liquid container materials	0.8 –1694[a]	*(10,57,59,63,65, 68,69)*
Antimony (Sb)	Metalloid	Respiratory irritation and inflammation	–	0.9 –6.2	*(10,57,59)*
Zinc (Zn)	Transition metal	Respiratory toxicity	Parts of heating elements (wicks, sheaths, joints), contamination in e-liquid ingredients; leaches from e-liquid container materials	0.4 –3250	*(10,57,59,63,70)*

LOD, limit of detection

[a] The upper reported range of metal content in 1 mL of e-liquid is comparable to or exceeds the content of the element in 1 g of cigarette tobacco. Ranges in US cigarette tobacco: Ct, 1400–3200 ng/g tobacco; Ni, 2100–3900 ng/g tobacco; Pb, 600–1160 ng/g tobacco *(71)*.

7.5.1.1 Factors associated with higher metal concentrations in e-liquids

See Table 7.4 for the potential effects of specific metals discussed in this section.

Contact of e-liquid with the metal-containing parts of e-cigarette device. Consistent with the expectation that device parts (e.g. coils, wick) are major sources of metals in e-liquids, the levels of metals are generally higher in closed systems (i.e. e-cigarette devices prefilled with e-liquid) than in e-liquids sold in separate bottles. For example, a study of 236 product samples purchased in four countries (Australia, Canada, England (United Kingdom) and the USA) showed that, although the flavour, the year and the country of purchase were significantly associated with levels of metals in e-liquids, the type of e-cigarette device had the most impact *(72)*. High concentrations of Pb, Ni and Cr were found only in closed-system samples. Similar findings were reported in another study, in which Pb was found in liquids from disposable e-cigarette devices but not in e-liquids sold in separate containers (bottles) *(69)*.

Studies of the impact of the duration of contact of e-liquid with the device provide further evidence that metals leach into e-liquids from device parts. For example, in a study of commercially available e-liquid samples in Romania, the concentrations of Pb, Ni, Zn and Co were compared immediately after purchase and after storage in "clearomizers" for 1, 3 and 5 days at a temperature of 22 °C or 40 °C *(73)*. For most metals, the longer storage duration and higher temperature were associated with higher concentrations of metals in e-liquids.

Coil type. It is axiomatic that the types and the concentrations of metals that leach from coils into e-liquids depend on the coil composition. For example, a study was conducted in Canada of leaching of Cr, Ni, Pb and Cd from coils made of kanthal, nichrome or stainless steel or of the commercial disposable coil brands Aspire BVC and Juul *(74)*. Different coils leached different amounts of the same metal when in contact with the same e-liquid, Ni and Cr being the predominant leached metals. The lowest level of leaching was observed from the stainless-steel coil. Coil ageing and different coil designs (e.g. double coil) can also impact metal transfer from coil to e-liquid.

Operation (heating) of devices. While simple contact of an e-liquid with device parts can lead to leaching of metals, operation of the device (i.e. heating of coils and other parts) appears to enhance this process. For example, a comparison was conducted of the levels of various metals (Zn, Pb, Ni, Fe, Cd and Cr) in the same e-liquids under three conditions: taken out of bottles, stored inside a device without puffing and taken out of the device after puffing *(75)*. A key finding of this study was that, except for Cd, the levels of all other metals in e-liquids were increased after puffing, with increases of 36–463 times, depending on the metal. The impact of heating on the transfer of metals from coils to e-liquids was also demonstrated in a laboratory setting, by heating coils in the presence of e-liquids *(76)*.

Composition of e-liquid. Several studies suggest that the nicotine concentration, the type of organic acid (for nicotine salt-based e-liquids) and flavours influence the extent of metal leaching into e-liquid. For example, elevated concentrations of nicotine were shown to enhance Cr, Ni, Fe, Cu, Zn and Pb leaching from coils to e-liquids *(74,76)*. An e-liquid made with benzoic acid leached greater concentrations of Cr and Ni from the same coil than an e-liquid made with glycolic acid *(74)*. Some fruit- and mint-flavoured closed-system products had higher metal concentrations than tobacco-flavoured products *(72)*. The effects of nicotine concentration and acid type are probably due to their corrosive effects on coils and other metal-containing devices. Furthermore, glycerol might result in greater transfer of metals from coils to liquids than its mixture with propylene glycol or propylene glycol alone *(76)*. In another study, however, the ratio of propylene glycol to glycerin in e-liquids did not significantly affect metal transfer *(74)*.

7.5.1.2 Transfer of metals from e-liquids to aerosols

Many of the factors that contribute to greater leaching of metals into e-liquids are also associated with higher levels of metals in e-cigarette aerosols. Further, the levels of metals in e-liquids appear to be indicative of the levels of these metals in aerosols *(77)*. These observations suggest that measures to reduce metal contamination of e-liquids will decrease users' exposure to metals in e-cigarette aerosols.

Device operation conditions. Factors such as higher device power settings, greater puff number and longer duration of device use (ageing) have been associated with higher emissions of many metals in e-cigarette aerosols *(78–81)*. The reports on the impact of puff duration on metal levels in aerosols are not, however, consistent, some claiming an increase *(79)* and others reporting no effect *(78)*.

Composition of e-liquid. Like the metal levels in e-liquids, the extent to which metals leaching from device parts transfer to aerosol e-liquid may be affected by the e-liquid composition. For example, the concentrations of Ni, Zn, Cu and Cr were higher in aerosols generated from e-liquids containing lactic acid than from the aerosols of e-liquids containing benzoic acid or laevulinic acid *(60)*. Further, the concentrations of some (but not all) metals in e-cigarette aerosols are positively associated with nicotine concentration *(79)*. This could be due either to a common source of nicotine and metals in the e-liquid (e.g. the tobacco plant from which nicotine was extracted) or to device operation settings that result in a more concentrated aerosol (e.g. higher wattage). The levels of metal are also higher in some flavour mixtures *(78,79)*.

Direct comparisons of metal concentrations in e-liquids and aerosols. Comparison of metal concentrations in e-liquids and aerosols could shed light

onto the sources and the mechanisms of the occurrence of metals in e-cigarette aerosols. For example, Olmedo et al. *(81)* analysed 15 metals in e-liquids from device tanks after e-cigarette use and in aerosols of e-cigarettes sold in Spain. The authors reported consistently higher levels of most metals in e-liquids than in aerosols from the same device, suggesting that metals are first leached into e-liquid and subsequently transferred to the aerosol. The exceptions were metals that are likely to be present in e-liquids as contaminants from sources unrelated to device parts (e.g. from e-liquid ingredients and preparation processes). These included Cd, As and Hg, the concentrations of which were similar in e-liquids and aerosols *(81)*. Slightly different findings were reported, however, in another recent study *(82)*, in which the Cr and Ni concentrations were greater in the aerosol than in the tank e-liquid. The authors concluded that these elements are directly transferred to the aerosol during heating of the nichrome coil element. The reasons for the discrepancies between these studies are not clear; however, differences in the device types (including coil composition) and e-liquid characteristics may have played a role.

7.5.2 Characteristics of metals in e-liquids

The physicochemical characteristics of some metals found in e-liquids are summarized in Table 7.5.

Table 7.5. Fundamental characteristics of some metals found in e-liquids

Metal	Atomic weight	Melting-point, ˚C	Boiling-point, ˚C	Density, g/cm³	Conductivity[a]		Reactivity	Oxidation
					Thermal, W/mK	Electrical, S/m		
Al	26.98	660	2467	2.70	237	3.8×10^7	Reacts with acids and bases to form salts	Forms Al oxide at high temperatures
As	74.92	817	613	5.75	35	3.3×10^6	Reacts with mineral acids to form toxic gas (arsine)	Oxidizes in the presence of moisture and at high temperatures
Cd	112.4	321	765	8.65	92	1.4×10^7	Reacts with strong acids (to form hydrogen gas); dissolves in dilute mineral acids	Reacts with oxidizing agents
Co	58.93	1495	2870	8.86	100	1.7×10^7	Dissolves in dilute mineral acids, releasing hydrogen gas; dissolves in dilute mineral acids	Oxidizes at elevated temperatures or in the presence of moisture

Metal	Atomic weight	Melting-point, °C	Boiling-point, °C	Density, g/cm³	Conductivity[a]		Reactivity	Oxidation
					Thermal, W/mK	Electrical, S/m		
Cr	51.99	1907	2672	7.19	94	7.9×10^6	Dissolves in dilute mineral acids, forming hydrogen gas; reactivity increases with heat	Forms oxides, can occur in several oxidation states
Cu	63.55	1084	2562	8.96	401	5.9×10^7	Low reactivity metal	Easily oxidized when exposed to air
Fe	55.85	1538	2861	7.87	80	1.0×10^7	Reactive with various compounds, forms organometallic compounds	Easily oxidized, a range of oxidation states
Mn	54.94	1250	2061	7.3	7.8	6.2×10^5	Dissolves in dilute mineral acids	Oxidizes to form various oxides
Ni	58.69	1455	2730	8.91	60.7	1.4×10^7	Moderate reactivity, reacts with mineral acids	Forms oxides, can occur in several oxidation states
Pb	207.2	328	1749	11.3	33	4.8×10^6	Reacts slowly with mineral acids	Forms oxides, can occur in several oxidation states
Sb	121.76	631	1587	6.68	18.6	2.5×10^6	Relatively unreactive at room temperature, but reactivity increases when heated	Oxidizes at high temperatures, can occur in several oxidation states
Zn	65.38	420	907	7.13	129	1.7×10^7	Dissolves in dilute mineral acids, forming hydrogen gas; reactivity increases with heat	Occurs primarily in a +2 oxidation state

[a] Conductivity units: W/mK = Watts per metre-Kelvin, a measure of thermal conductivity; S/m = Siemens per metre, a measure of electrical conductivity. These measures reflect the ability of a metal or metalloid to conduct heat and electricity, respectively.
Source: Kim et al. *(21)*

7.5.3 Determination of metals in e-liquids

Various methods can be used to measure metals in e-liquids. A common analytical technique is inductively coupled plasma mass-spectrometry (ICP-MS) *(57,67,77,79)*, which is often preferred due to its selectivity and sensitivity (limit of detection, 1–10 parts per trillion). Sample preparation typically requires digestion in strong acid (e.g. nitric acid). As ICP-MS instruments can be prohibitively expensive, other analytical techniques have been successfully used for metal analyses, which include ICP-optical emission spectrometry *(83)*, graphite furnace

atomic absorption spectrometry *(69)* and total reflection X-ray fluorescence spectroscopy *(64,84)*. Some characteristics of these methods are summarized in Table 7.6. In addition, a new method based on fluorescent signal enhancement of rhodamine B dye has been developed for Pb(II) trace analysis in e-cigarette liquids, with results validated by ICP-MS *(68)*. In all these methods, care must be taken during sample preparation to prevent leaching of metals into the sample from sample preparation materials.

Table 7.6. Examples of methods used for metal analysis in e-liquids

Method	Limit of detection	Examples of advantages	Disadvantages	Examples of studies
Inductively coupled plasma mass-spectrometry	Parts per trillion	High sensitivity, high throughput (all elements in 2–6 min), wide linear dynamic range, allows for isotope analysis	Very high cost, requires specialized skill	*(57,67,77,79)*
Inductively coupled plasma-optical emission spectrometry	Parts per billion	Relatively high sensitivity, relatively high throughput (5–30 elements per min); wide linear dynamic range	Relatively high cost, requires specialized skill	*(83)*
Graphite furnace atomic absorption spectrometry[a]	Parts per billion	High sensitivity, more affordable than the two preceding methods	Longer analysis times (4 min per element), narrower linear dynamic range	*(72)*
Total reflection X-ray fluorescence spectroscopy	Parts per billion range	Minimal sample preparation, short analysis time (a few seconds to a few minutes); relatively low cost	Potential matrix effects (reduced selectivity), limitations of analysing complex samples	*(64,84)*

[a] Also known as electrothermal atomic absorption spectroscopy

7.5.4 Toxicity implications of the presence of metals in e-liquids

7.5.4.1 Exposure of e-cigarette users to metals

Two recent reviews summarized data on biomarkers of metal exposure in people who use e-cigarettes. The review by Batista et al. *(85)* addressed only metals in 18 studies in which metal biomarkers were reported for users and non-users exposed to secondhand e-cigarette aerosols. The second review was a general scoping review of biomarkers of exposure associated with e-cigarette use, including metal biomarkers *(86)*. In both studies, it was concluded that there was substantial evidence that exclusive users of e-cigarettes are exposed to higher levels of biomarkers of certain metals (e.g. Cd, Pb and Se) than non-users. Examples of findings for specific metal biomarkers are provided below.

Cadmium. Although the results on the levels of Cd biomarkers in e-cigarette users are mixed, comparisons with non-users and cigarette smokers provided substantial evidence that e-cigarette users have higher exposure to Cd than non-users *(85–89)*. A few studies, however, reported no difference among smokers, e-cigarette users and non-users *(90,91)*. The smoking histories of participants were not collected in all the studies, however, which could have

affected the outcomes of those in which urinary Cd was assessed, as the half-life of urinary Cd may be as long as 38 years.

Cobalt. Published studies suggest no difference in the levels of urinary Co in e-cigarette users, smokers and non-users *(87,90)*.

Chromium. Reports on Cr levels in e-cigarette users are inconsistent. One study indicated that exclusive e-cigarette users have higher levels of urinary Cr than non-users and that the level of salivary Cr is correlated with Cr levels in e-cigarette aerosols *(91)*, while another study found no difference in urinary Cr between cigarette smokers, e-cigarette users and non-users *(92)*.

Lead. Most studies of urinary and blood Pb levels in e-cigarette users found no difference from those in cigarette smokers or non-users *(85);* however, data from wave 1 of the PATH study *(87)* showed that urinary Pb in e-cigarette users was significantly higher than in non-users. In addition, data on adolescents from wave 5 of the PATH study showed that frequent and intermittent e-cigarette users, defined as using e-cigarettes for 6–19 days and for > 20 days, respectively, over the past 30 days, had higher urinary Pb than occasional users (1–5 days of e-cigarette use over the past 30 days) *(93)*.

Manganese. No indication was found that urinary or blood Mn differs between e-cigarette users, smokers and non-users *(85,87)*.

Nickel. Reports on Ni levels in e-cigarette users are discrepant. One study reported that exclusive e-cigarette users have higher levels of urinary Ni than non-users, while salivary Ni levels correlated with those in e-cigarette aerosols and with product use patterns *(91)*. Another study reported no difference in urinary Ni between cigarette smokers, e-cigarette users and non-users *(92)*.

Zinc. Results of cross-sectional studies show that urinary and blood Zn levels in exclusive e-cigarettes users are significantly higher than in non-users and are comparable to those in smokers *(85,94)*.

As mentioned earlier, some of the discrepancies between biomarker studies might be attributable to differences in the tobacco use histories (e.g. former cigarette smoking) of the e-cigarette users. Other potential factors are the variability of e-cigarette brands and device types and/or the patterns of e-cigarette use.

7.5.4.2 Toxic and carcinogenic effects of metals in e-cigarettes

Many metals are potent toxicants and carcinogens in organs in the human body. For example, Cd is a known lung, kidney and potentially prostate carcinogen, and a statistically significant association was reported between urinary Cd levels and lung cancer mortality in men in the third US National Health and Nutrition Examination Survey cohort *(95–97)*. Cr, Ni and As are also carcinogens, and their inhalation is associated with cancers of the lung and nasal cavity *(98–100)*. Cd and Ni can also act as metalloestrogens, and exposure to Cd has been linked to oestrogen receptor-positive breast cancer in epidemiological studies *(101,102)*. In addition, inhalation

of As, Pb, Cd, Cu and other elements has been associated with increased risks for respiratory and cardiovascular diseases and coronary heart disease *(103–107)*.

While no studies have directly linked exposure to metals in e-cigarettes to specific health outcomes, a recent study addressed toxicity end-points, including cancer and non-cancer risk assessment, after such exposure *(108)*. The risks were estimated from published data on metal concentrations in e-liquids and aerosols (Table 7.7). In view of their prevalence and abundance, Cr and Ni were determined to be the leading contributors to cancer risk, with Cd, Pb and As contributing to only a minor extent. At an assumed consumption of 2 mL e-liquid per day, the risks ranged from 5.7 to 30 000 additional cancers in one million e-cigarette users. Non-cancer risks were estimated in the "hazard quotient" approach. For estimated exposure at the maximum reported concentrations to Ni, Cr and Mn, the hazard quotients were 161, 1.1 and 1.0, respectively. (Note: a hazard quotient > 1.0 indicates possible non-cancer adverse health effects.) With the well-established mechanistic, laboratory animal and epidemiological data on the health effects associated with metal exposures, this risk assessment indicates that exposure to metals during use of e-cigarettes may pose a significant health risk at the mid and upper end of the reported ranges. Therefore, reduction of metals in e-liquids would protect public health. While such risk assessment calculations are based on a number of assumptions, such as daily intake and body weight, and the results of biomarker studies to date are inconclusive, some of these estimates of health risk are comparable to or higher than those reported for smoking cigarettes. For example, the mean cancer risk due to exposure to Cr while smoking cigarettes was estimated to be 2.95×10^{-3} *(109)*. There have, however, been no direct comparisons of the estimated risk of exposure to metals of smokers and e-cigarette users.

Table 7.7. Estimated cancer and non-cancer risks of some metals in e-cigarettes according to published data on their levels in liquids and/or aerosols

Metal	Cancer potency slope factor[a] $(\mu g/kg/day)^{-1}$	Estimated cancer risk[b]		Non-cancer REL[b] ($\mu g/m^3$)	Non-cancer hazard quotient		Target system
		Intake at average reported levels	Intake at maximum reported levels		Intake at average reported levels	Intake at maximum reported levels	
Cr	0.51	2.55×10^{-4}	2.53×10^{-3}	0.2	2.13×10^{-1}	$2.11 \times 10^{+0}$	Respiratory system
Ni	0.00091	9.67×10^{-5}	1.08×10^{-3}	0.014	–	–	Respiratory, immunological systems
Pb	0.000042	2.87×10^{-7}	1.96×10^{-6}	0.15	1.61×10^{-1}	$1.09 \times 10^{+0}$	CNS, reproductive, development
As	0.012	5.15×10^{-6}	2.15×10^{-5}	0.015	1.64×10^{-3}	6.83×10^{-3}	Development, cardiovascular, CNS, respiratory
Cd	0.0015	8.60×10^{-7}	1.72×10^{-6}	0.02	1.90×10^{-4}	3.81×10^{-4}	Kidney, respiratory
Mn	NA	NA	NA	0.09	3.32×10^{-1}	$1.84 \times 10^{+0}$	CNS

Source: adapted from Fowles et al. (108)

Values in bold indicate a significant risk.

[a] Cancer slope factors and reference exposure levels (REL) used in the source are from California Environmental Protection Agency and the US Environmental Protection Agency.

[b] Cancer risk estimates were calculated by multiplying cancer potency by the estimated daily intake from 2 mL of e-liquid.

7.6 Regulation of aldehydes and metals in nicotine and tobacco products

In the partial guidelines for implementation of Articles 9 and 10 of the WHO FCTC guidelines *(1)*, Member States are advised to adopt comprehensive tobacco control measures, which may include regulation of constituents or ingredients that contribute to the attractiveness, addictiveness or toxicity of products. As summarized above, aldehydes added to e-liquids as flavouring additives contribute to the attractiveness of e-cigarettes and potentially to their addictiveness and toxicity. Toxic and carcinogenic metals in some e-liquids are a source of user exposure to comparable or even higher levels of these elements than in smoking.

As of the time of writing of this report, no specific regulatory measures are in place to limit exposure to these constituents in e-liquids. Some countries have, however, either implemented or proposed regulation of additives in tobacco and nicotine products, which should include flavouring agents (see Chapter 3 "Flavours in tobacco and nicotine products: new developments, implications and regulation") such as the aldehydes discussed in this paper.

Bans on flavours in e-cigarettes other than tobacco flavour are in place in countries including China, Finland, Sierra Leone, Slovenia and Ukraine. Nevertheless, tobacco-flavoured additives can still contain aldehydes and be appealing to users.

Proposed or upcoming bans on flavours in e-cigarettes. The European Tobacco Product Directive imposes a ban on flavours in e-cigarettes *(110)*, and the measure is expected to take effect in 2025. In 2021, Health Canada proposed new regulations to restrict e-cigarette flavours *(111)*; however, the measure has not yet been implemented.

Bans on additives and flavours in other products. Examples of such bans include a ban in the European Union on characterizing flavours in cigarettes and roll-your-own products, which was imposed in 2014 (Directive 2014/40/EU) *(110)*. In addition, product manufacturers are required to disclose (annually) the composition of all marketed tobacco products. Many additives in cigarettes were banned by Health Canada in 2009 (amendment to the Tobacco Act, Bill C-32) *(112)*, which also require manufacturers and importers to provide information on all tobacco product ingredients. Under the authority granted in 2009 by the US Family Smoking Prevention and Tobacco Control Act, the Food and Drug Administration banned cigarettes containing characterizing flavours except menthol *(113)*; however, the ban does not extend to e-cigarettes.

7.7 Summary and conclusions

Key takeaways on aldehydes

- The major aldehydes present in e-liquids and/or associated aerosols are vanillin, ethyl vanillin, benzaldehyde, formaldehyde and acetaldehyde. They can contribute to the attractiveness, addictiveness and toxicity of e-cigarettes. They arise from addition as flavourants or in aerosol as decomposition products formed during heating.
- Most of the aldehydes used in e-liquids as flavouring additives have been extensively tested and evaluated as generally regarded as safe for their intended use in food. Such testing and classification are not, however, directly applicable to the route of exposure of e-cigarette users, which is inhalation.
- The presence of aldehydes in aerosols, particularly formaldehyde, acetaldehyde and acrolein, is a significant toxicological concern related to e-cigarette use. These aldehydes are established carcinogens, and the amounts of acrolein–DNA adducts are significantly higher in e-cigarette users than in non-users of any tobacco or nicotine product.

Key takeaways on metals

- At least 35 metals have been reported to be present in e-cigarette liquids and aerosols. All e-liquids in contact with e-cigarette devices contain Ni, Cr and some other metals as a result of leaching from the coils and other device parts. E-liquids also contain metals as contaminants, and Cd, Pb and As have been commonly reported.
- The levels of metals in e-liquids vary dramatically, depending on the types of coils and other metallic parts of the device and on e-liquid composition. Such product characteristics can be controlled to minimize metal transfer from the device to the aerosol.
- Metals transfer from e-liquid to aerosol during product use. Some biomarker studies show that exposure to Cr, Cd, Pb, Zn and other metals may be higher in e-cigarette users than in non-users and/or are comparable to exposures in smokers. However, the findings are inconsistent.
- No direct assessments of the effect of metals in e-liquids on health outcomes in users were identified. There are, however, well-established mechanistic, laboratory animal and epidemiological data on the health effects associated with exposure to metals. A risk assessment concluded that exposure to metals from use of e-cigarettes may pose a significant health risk at the mid- and upper ends of the reported ranges.

7.8 Research directions

Several research directions could further elucidate the impact of aldehydes and metals in e-liquids on exposure and disease-relevant effects in users:

- more comprehensive data on aldehydes in e-liquids in addition to those on the Dutch market;
- more data on the pathways of aldehydes in e-liquids during product use (aerosol emissions): decomposition and percentage transfer as intact chemicals; and inhalation toxicology of flavouring additives, particularly vanillin, ethyl vanillin, benzaldehyde and of their decomposition products;
- studies to determine product characteristics that minimize generation of known aldehyde toxicants and contamination of e-liquids with metals;
- better characterization of human exposure to metals from use of e-cigarettes, with appropriate biomarkers;
- comprehensive global surveillance of e-cigarette constituents, including those formed from flavour compounds, and their toxicological profiles; and
- more studies of the dose–response relations of aldehydes and metals in e-liquids, particularly when inhaled, to better characterize their toxicity and for establishment of evidence-based limits.

7.9 Policy recommendations

The following specific policy recommendations are proposed:

- mandated banning of aldehydes, such as acetaldehyde and acrolein, as flavouring additives, with no exception for tobacco flavours;
- mandated disclosure of all ingredients in e-cigarette liquids;
- mandated disclosure of constituents in e-liquids measured, when applicable, with WHO TobLabNet methods; and
- support for research independent of the tobacco industry on the composition, appeal, addictiveness and toxicity of e-cigarettes.

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8. Smokeless tobacco: a complex landscape, product regulation and considerations for the future

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Contents

Abstract
8.1 Introduction
8.2 Methods
8.3 Overview of products
8.3.1 Types of SLT products
8.3.2 Characteristics of SLT products
8.4 A complex landscape
8.4.1 Case studies of product marketing
8.4.2 Health impact and cessation
8.5 Regulation and future considerations
8.5.1 Regulatory challenges
8.5.2 Regulatory landscape
8.5.3 Examples of studies on regulation of SLT
8.5.4 Opportunities and considerations for the future
8.6 Research gaps, priorities and questions
8.7 Policy recommendations
References

Abstract

An estimated 359 million people across 140 countries around the world use smokeless tobacco (SLT). A majority of these users (80%) reside in the Southeast Asia region. While cigarette smoking is decreasing in most countries, SLT use is on the increase, particularly in countries that already have a high burden of use. Use of SLT products is associated with a range of adverse health outcomes, including cancers (oral, oesophageal, pancreatic), oral potentially malignant disorders, diabetes, and cardiovascular diseases. The term encompasses a diverse array of products with different characteristics in use around the world, often mixing tobacco with other ingredients, including flavorings. SLT products also contain nicotine, which is addictive.

However, control of SLT use lags behind that for cigarettes and other smoked tobacco products in many countries, and SLT poses unique challenges to regulation different than those for conventional smoked tobacco products, including the diversity of products and sometimes informal modes of production.

Case studies from multiple countries highlight how tobacco manufacturers have developed novel products, manipulated nicotine content, and used sophisticated marketing techniques to reach new users, particularly youth and young adults.

There are examples from a number of countries of promising efforts to regulate SLT products, such as through restrictions on added flavourings, bans on particular product classes (such as gutka in India), and use of graphic warning labels. Additionally, there are examples of successful national media campaigns against SLT use from India and the U.S. Recent systematic reviews have found that behavioural interventions are successful in promoting cessation of SLT use among adults and limited emerging evidence for pharmacologic interventions. The WHO FCTC and other tobacco control measures should be fully implemented to put SLT products at par with smoked tobacco products, with particular attention to reducing SLT use among youth.

Keywords: smokeless tobacco, carcinogens, product regulation, youth tobacco use, tobacco industry

8.1 Introduction

It has been estimated that over 359 million people aged > 15 years around the world use SLT *(1)*. Most of these users (80%) live in the WHO South-East Asia Region (mainly Bangladesh and India), although SLT is also a substantial global health problem *(2)*. Moreover, while cigarette smoking is decreasing in most countries, SLT use is on the increase, particularly in countries that already have a high burden of tobacco smoking. Use of SLT products is associated with various adverse health outcomes, including oropharyngeal, oesophageal and pancreatic cancers; potentially malignant oral lesions; diabetes mellitus; cardiovascular diseases; low birth weight; and preterm birth *(3)*. The IARC and the WHO TobReg have both reported wide variation in the type and extent of disease caused by use of SLT and that the dissimilarities in the disease risks observed were associated with large differences in the concentrations of carcinogens in the tobacco used and in patterns of use. In its fifth, sixth and seventh reports*(4–6)*, TobReg recommended measures that might reduce the attractiveness, addictiveness and toxicity of SLT products, including controlling the contents of the products and mandating disclosure.

The WHO FCTC *(7)* was a landmark, as it was the first global public health treaty. The WHO FCTC was enacted to combat the challenges posed by the tobacco epidemic. Article 1(f) of the Convention defines tobacco products as including all "products entirely or partly made of the leaf tobacco as raw material which are manufactured to be used for smoking, sucking, chewing, or snuffing." Article 4.4 of the Convention states that comprehensive measures to reduce consumption of all tobacco products are essential to prevent the incidence of

diseases, premature disability and mortality due to tobacco use. In the Report by the Working Group on Articles 9 and 10 *(8)*, presented at the seventh session of the COP of the WHO FCTC in August 2016, SLT products were stated as "to be considered tobacco products, as per the definition set out in the WHO FCTC". Further, in the report by the Convention Secretariat presented at the fourth session of the COP in September 2010 *(9)*, the term SLT is used to describe tobacco that is "consumed in unburnt form, either orally or nasally". With changing products and modes of use, such definitions will be revised periodically. In this report, we built on definitions of SLT in previous reports and decisions of the WHO FCTC COP and in reports from the WHO Study Group on Tobacco Product Regulation, as follows:

> Smokeless tobacco products are made entirely or partly from tobacco or its extracts and are consumed in unburnt form at the time of use. Such products are used in a variety of ways, including being chewed, sucked or just held between the lip/cheek and gums, applied to the teeth or gums (e.g. topical toothpaste or powder), dissolved in the mouth or applied directly to the body (e.g. the skin).

In this report, the SLT products considered are limited to those containing tobacco and to conventional categories, not including nicotine pouches. Product characteristics and regulation of nicotine pouches are addressed in the ninth Report of the WHO Study Group on Tobacco Product Regulation *(10)*.

As recognized in the report by WHO to the sixth session of the Conference of the Parties to the WHO FCTC, in May 2014, "the problem of SLT use is no longer a local or regional problem but a major global one affecting a large percentage of the world's population" *(11)*.

The term "SLT" encompasses a diverse array of products with different characteristics and composition, different modes of preparation (e.g. manufactured and hand-made) and patterns of use around the world. These include manufactured products, including chewing tobacco, snuff, *gutka*, snus and tobacco lozenges, and hand-made preparations, such as betel quid with tobacco, *toombak*, *iqmik* and tobacco water (*tuibur*). Consideration must also be given to the health impact of carcinogenic non-tobacco products that are frequently used in conjunction with SLT, such as areca (betel) nut, and also to the health and social impact of flavourings added to SLT products. More information regarding flavours and flavouring agents, is provided in "Flavours in tobacco and nicotine products: new developments, implications and regulation" in this report.

Regulation of SLT products has generally lagged behind regulation of cigarettes. In many countries, tobacco control interventions and policies have not been applied to SLT or applied less, including restriction on attractive flavours that may be prohibited in cigarettes. Many countries also do not have mandated

graphic health warnings on their packaging and SLT are often excluded from policies for tobacco-free workplaces and public spaces. Recent reviews of global tobacco control policies have shown gaps in implementation of WHO FCTC policies for SLT products, particularly in high-burden low- and middle-income countries (LMIC) *(12,13)*.

Several issues specific to SLT pose challenges to their regulation:

- The wide range of products available: Understanding the use and impact of SLT is complicated by the diversity of products, mode of use and user behaviour.
- Evolving product market: During the past few decades, SLT product manufacturers have continually introduced new product formulations and used new marketing techniques to appeal to new users, including by manipulating nicotine content, using attractive flavourings and developing products that can be used discreetly, including "dissolvables", which are essentially tobacco pressed into tablets, rods or flat strips that fully dissolve in the mouth and may also contain adhesives, binders and whiteners, to be used in situations or in places that cigarette smoking is not allowed.
- Modes of production: Products may be mass produced, manufactured by a local informal industry or assembled from raw ingredients at the point of sale. Informal cottage industry production methods and assembly by street vendors create unique challenges for regulation because of the lack of standardized methods and products.
- Variable assessments of health risks: While many studies have shown adverse outcomes in SLT users, including an increased risk for oral cancer, the magnitude of the health risks directly associated with SLT differs from that for smoking and appears to differ by country and region, due in part to differences among products and use patterns *(3)*.
- Limited data: Given the diversity of products and modes of use, limited data are available on the properties of these products, how they are consumed and what consumers are exposed to. Additionally, while some countries have recent estimates of national prevalence from surveys, others have no recent national data that include SLT use, which presents challenges for monitoring use over time and assessing the scope of the problem. The lack of standardized measures also creates challenges for defining and monitoring the wide variety of products in use.
- Regulation and control: Regulations for preventing and controlling SLT use lag behind those for cigarettes and other smoked tobacco products in many countries *(12,13)*.

8.2 Methods

Published sources, reports and data on SLT were used. The sources included reports from WHO, including previous TobReg documents and the WHO Report on the global tobacco epidemic, global progress reports on implementation of the WHO FCTC, IARC monographs and reports of country government agencies, including the Indian Ministry of Health and Family Welfare and the US National Cancer Institute. Other data sources included the Global Adult and Youth Tobacco Surveys, the WHO STEPwise approach to NCD risk factor surveillance surveys and the Demographic and Health Surveys.

The authors also reviewed the global scientific peer-reviewed literature relevant to SLT in PubMed, including reports of clinical and laboratory studies, surveys and epidemiological studies, studies of tobacco industry activities and marketing and studies of SLT regulation and control. The search terms included "smokeless tobacco", "smokeless", "oral tobacco", "snus", "chewing tobacco", "snuff", "gutka" and "betel quid". Information on tobacco product regulation was also obtained from selected national government agencies. The search and analysis were conducted between June and December 2024. Data on prevalence and regulation were updated during the review from the WHO report on the global tobacco epidemic 2025 *(14)* and the WHO global report on trends in prevalence of tobacco use 2000–2024 and projections 2025–2030 *(1)*.

8.3 Overview of products

8.3.1 Types of SLT products

A vast array of SLT products is available. A summary of products, ingredients and use by WHO region is presented in Volume 100E of the IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, "Personal habits and indoor combustions" *(15)*. The various modes of use, such as chewing, sucking, gargling, applying to the teeth or gums or inhaling into the nostrils, are presented with a list of ingredients and the WHO regions and countries in which the products are used. Intravaginal insertion of tobacco has been reported in sub-Saharan Africa *(16)*.

Examples of commonly used products and their modes of use by WHO region include: *chimo* (sucking, Region of the Americas), *iqmik* (chewing, Region of the Americas), dry snuff (sucking, worldwide), *gutka* (sucking, South-East Asia Region), *khaini* (sucking, South-East Asia Region), loose-leaf (chewing, Region of the Americas, European Region), *mishri* (sucking, South-East Asia Region), moist snuff (sucking, Region of the Americas, European Region), *naswar*/*nass* (sucking, African Region, Eastern Mediterranean Region), snus (sucking, Region of the Americas, European Region), *zarda* (chewing, South-East Asia Region, Eastern Mediterranean Region), dry snuff (sniffing, African Region, South-East Asia Region, European Region, Eastern Mediterranean Region); and betel quid

with tobacco, commonly known as *paan* or *pan*, consisting of betel leaf, areca nut, slaked lime and tobacco (chewing, South-East Asia Region, Eastern Mediterranean Region). The sixth report of WHO TobReg *(5)* provides a thorough survey of the characteristics of SLT products used around the world.

Photographs of SLT products are presented in Smokeless tobacco and public health: a global perspective by the US National Cancer Institute *(3)*, which includes a useful summary of the characteristics of products that are manufactured, custom made (cottage industry) or custom made (vendor or individual). Examples of manufactured products, which are mass produced and sealed in labelled commercial packaging, are moist snuff, dry snuff, *gutka*, *khaini* and chewing tobacco, while custom-made products are made by hand in non-traditional environments and sold in non-commercial packaging. They include such products as *nass*, betel quid with tobacco and *toombak*. Custom-made products are made on site by a vendor according to individual preferences. They include products such as *gudahku*, *shammah*, and betel quid with tobacco. The manufactured products are mass produced commercially and marketed throughout the world.

8.3.2 Characteristics of SLT products

Nicotinia tabacum and sometimes *N. rustica*, two of the three main subgenera of the genus *Nicotiana*, are used in SLT products. They are often combined with other ingredients, as noted above for *paan*. The IARC Monograph on the Evaluation of Carcinogenic Risks to Humans, Vol. 89 *(17)* noted that one type of smokeless tobacco, *chimó,* contains tobacco leaf, sodium bicarbonate, brown sugar, ashes from the mamon tree and vanilla and anisette flavourings. Dry snuff is fire cured, then fermented and processed into a dry, powdery form. *Gutka* consists of sun-dried, roasted, finely chopped tobacco, areca nut, slaked lime and catechu mixed with flavourants and sweeteners. *Khaini* is made from sun-dried or fermented leaves from *N. rustica* and/or *N. tabacum*. The leaves are crushed, and a pinch is mixed with slaked lime paste. Loose-leaf tobacco consists of loose tobacco leaves that are air cured, stemmed, cut or granulated and loosely packed to form small strips of shredded tobacco, sweetened and flavoured with liquorice. *Mishri* is made from toasted or partially burnt tobacco that is powdered for use. Moist snuff is either air-cured or fire-cured and processed into fine particles or strips. *Naswar* is a mixture of sun-dried, powdered *N. rustica* tobacco, ash, oil, flavourings, colouring agents and sometimes slaked lime pounded and mixed, then mixed with water and rolled into balls. Snus is a Swedish moist snuff consisting of finely ground dry tobacco mixed with flavourings, water, humidifying agents and sodium carbonate. *Zarda* is made of tobacco, lime, spices and vegetable dyes. The tobacco leaves are broken and boiled with the lime and spices, and the mixture is dried, coloured with vegetable dyes and mixed with finely chopped areca nuts and spices. Dry snuff consists of fire-cured tobacco which is then fermented and processed into a dry powder. It is

frequently used both orally and nasally. *Iqmik* is a mixture of tobacco and punk (*Phellinus igniarius*, a type of fungus) ash; it is used by Alaska natives *(18)*.

All these products are effective systems for delivering nicotine. The wide variety of products that have been used for centuries attest to the pharmacological and addictive powers of nicotine. The nicotine levels in SLT products vary widely, as does the pH, which determines the amount of free, unprotonated nicotine which is that most rapidly absorbed through the oral mucosa. In one study, the nicotine content of SLT products used in India ranged from 4.67 to 31.25 mg/g, and the pH from 5.20 to 10.07 *(19)*. The amount of unprotonated nicotine in a product can be calculated from the Henderson–Hasselbalch equation. In the study by Sharma et al. *(19)*, products with acidic pH (5.20–5.74) contained 0.12–0.26% unprotonated nicotine, while products with basic pH (8.17–10.07) had levels of 58.6–99.1%. In a review of commonly used SLT products *(20)*, the levels of nicotine in various products ranged from 0.2 to 48.7 mg/g and the pH from 4.7 to 11.6 (Table 8.1). Levels of nicotine up to 12%, have been reported in some *N. rustica* tobacco samples. A recent study of SLT products sold in the USA reported nicotine levels of 6.2–35.5 mg/g wet weight, of which 0.1–62% was unprotonated *(21)*. The importance of pH for nicotine absorption and how tobacco product manufacturers have manipulated pH levels to control products' nicotine delivery and addictiveness has been demonstrated *(22)*.

Table 8.1. Commonly consumed SLT products

SLT product	Region (WHO)	Countries with the highest consumption	Other ingredients	Preparation and use	pH	Nicotine (mg/g)	Total TSNA[a] (ng/g)
Snus (Swedish)	European	Norway, Sweden	Water, sodium carbonate, sodium chloride, moisturizers, flavouring	Heat treatment; placed between the gum and upper lip	6.6–7.2	7.8–15.2	601–723
Plug, snuff (USA), snus (USA)	Americas	Canada, Mexico, USA	Sweeteners, liquorice	Plug: air cured Dry or moist snuff: finely ground and fire cured Snus; steam cured Snuff: kept between lip and gum; dry snuff can also be inhaled	4.7–7.8	3.9–40.1	313–76 500
Chimó	Americas	Colombia, Venezuela	Sodium bicarbonate, brown sugar, mamon tree ashes	Tobacco paste made from tobacco leaves Placed between the lip or cheek and gum and left there for some time	6.9–9.4	5.3–30.1	9390

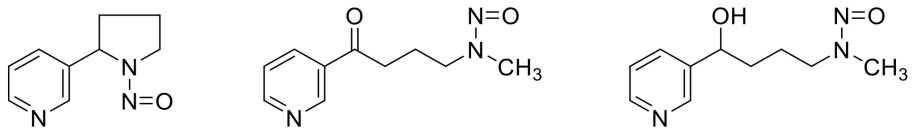
SLT product	Region (WHO)	Countries with the highest consumption	Other ingredients	Preparation and use	pH	Nicotine (mg/g)	Total TSNA[a] (ng/g)
Nass (*naswar*)	European and Eastern Mediterranean	Afghanistan, Islamic Republic of Iran, Kyrgyzstan, Pakistan, Tajikistan, Uzbekistan	Lime, ash, flavourings (cardamom), indigo	Sun-dried and powdered Placed between lip or cheek and gum	8.4–9.1	8.9–14.2	478–1380
Toombak	African and Eastern Mediterranean	Chad, Sudan	Mixed with moist sodium bicarbonate	Fermented and ground Placed and kept in mouth	7.3–10.1	9.6–28.2	302 000–992 000
Snuff (North and West African)	African	Algeria, Cameroon, Chad, Ghana, Nigeria, Senegal	Dried tobacco leaves mixed with potassium nitrate and other salts	Dry snuff Finely ground and inhaled as a pinch Moist snuff is placed in the mouth.	9.0–9.4	2.5–7.4	1520–2420
Snuff (South African)	African	South Africa	Dried tobacco leaves mixed with ash	Dry snuff Finely ground and inhaled as a pinch	6.5–10.1	1.2–17.2	1710–20 500
Khaini	South-East Asian, Western Pacific	Bangladesh, Bhutan. India, Nepal	Slaked lime, menthol, flavourings, areca nut	Shredded Kept in mouth between lips and gum	9.6–9.8	2.5–4.8	21 600–23 900
Zarda	South-East Asian, Eastern Mediterranean	Bangladesh, India, Indonesia, Maldives, Myanmar, Nepal, Pakistan, Sri Lanka, Thailand, United Kingdom	Wrapped in a betel leaf with slaked lime, catechu and areca nut	Shredded tobacco leaves boiled with lime and saffron; the mixture is dried then chewed and spat.	5.2–6.5	9.5–30.4	5 490–53 700
Gutka	South-East Asian	Bangladesh, India, Myanmar, Nepal, Pakistan, Sri Lanka, United Kingdom	Betel nut, catechu, flavourings, sweeteners	Commercially manufactured; sucked, chewed and spat	7.4–8.9	0.2–4.2	83–23 900

[a]TSNA, tobacco-specific nitrosamines
Figures adapted from Stanfill et al. *(23)*, Lawler et al. *(24)* and US National Cancer Institute *(3)*

All SLT products contain the TSNAs *N*'-nitrosonornicotine (NNN) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), which were evaluated as "carcinogenic to humans" by a working group convened by IARC *(17)*. They are widely considered to be the ingredients that link SLT use to cancer. NNK is extensively metabolized to 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), which is also highly carcinogenic. The structures of NNN, NNK and NNAL are shown in Fig. 8.1. Several other TSNA, namely *N*'-nitrosoanatabine (NAT), *N*'-nitrosoanabasine (NAB), 4-(methylnitrosamino)-4-(3-pyridyl)-1-butanol and 4-(methylnitrosamino)-4-(3-pyridyl)-butanoic acid have also been identified in SLT products but have received less attention, either because the levels at which they occur are relatively low or because they do not have strong

carcinogenic activity. Many studies have reported relatively high amounts of TSNA in SLT products. Table 8.1, which provides representative data for all TSNA and for NNN, NNK, NAB and NAT from international studies on various product types *(20)*, indicates that the lowest levels were 601–723 ng/g wet weight tobacco in Swedish snus and the highest were in Sudanese *toombak* (302 000–992 000 ng/g) and in SLT sold in the USA (313–76 500 ng/g). In a recent study of products sold in the USA, NNN and NNK were found at levels of 270–12 206 ng/g and 81–20 716 ng/g wet weight, respectively *(21)*.

Fig. 8.1. Structures of NNN, NNK and NNAL

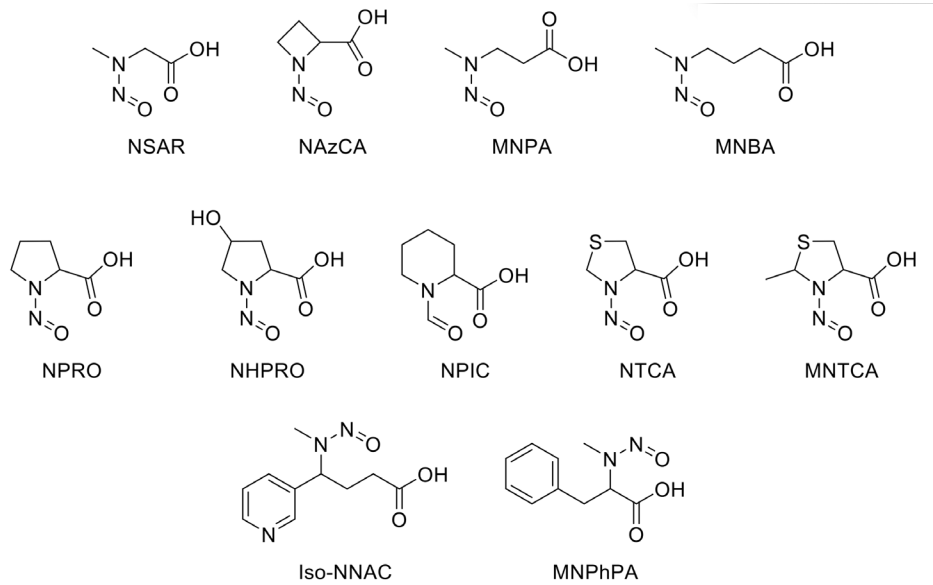


NNN NNK NNAL

NNN, NNK, and NNAL are potent carcinogens in animal models *(25)*. NNN causes tumours in the oral mucosa and oesophagus in rats, while NNK causes lung tumours in several animal models at low doses, independently of the route of administration. NNAL has similar carcinogenic activity to that of NNK *(26,27)*. A mixture of NNN and NNK caused oral tumours in rats *(28)*. In humans, the levels of the urinary NNK metabolite NNAL were significantly higher in SLT users than in cigarette smokers or in never-users of tobacco products in the USA *(29,30)*. The formation in tobacco and the toxicity and carcinogenicity of NNN and NNK were reviewed recently *(31,32)*. While the levels of specific product constituents and metabolites measured in SLT users vary widely, no recommended or "safe" threshold has been identified, although it is generally considered that lower levels of toxicants will reduce harmful exposures and the resulting health effects. The wide difference in levels could also be used in product regulation, as it suggests that toxicant levels in tobacco products can be reduced. Previous WHO TobReg reports have noted that toxicity could be reduced by setting product standards and imposing upper limits on key constituents such as TSNAs *(5)*.

Of the 11 *N*-nitrosamino acids identified in SLT (Fig. 8.2), 3-(methylnitrosamino)propionic acid (MNPA), 4-(methylnitrosamino)butyric acid (MNBA), *N*-nitrosoazetidine-4-carboxylic acid (NAzCA) and *N*-nitrososarcosine (NSAR) are carcinogenic. MNPA induced lung tumours in A/J mice *(33)*, MNBA caused bladder tumours in F344 rats *(34)*, and NSAR induced nasal tumours in mice and tumours of the oesophagus in rats *(35)*.

Fig. 8.2. Structures of N-nitrosamino acids identified in SLT



SLT can be contaminated with carcinogenic polycyclic aromatic hydrocarbons (PAH) such as benzo[*a*]pyrene (BaP) during fire-curing of tobacco or from air pollution near tobacco farms. A study of SLT products purchased in the USA found BaP at levels of 0.6–160 ng/g tobacco on a wet weight basis and NNN and NNK at concentrations of 276–10 473 ng/g and 79 to 28 882 ng/g, respectively *(36)*. Many PAH, including benz[*a*]anthracene, chrysene, benzofluoranthenes and BaP were quantified in SLT products in five African countries at amounts of 1–100 ng/g dry weight of tobacco *(37)*.

Formaldehyde and acetaldehyde are present in SLT products. Formaldehyde is considered to be carcinogenic in humans *(38,39)*, as is acetaldehyde found in alcohol. Formaldehyde was found in tobacco at levels of 0.13–5.67 µg/g and acetaldehyde at 0.33–6.9 µg/g tobacco on a wet weight basis *(36)*. A recent study indicated wide variation in the levels of carcinogenic metals in SLT products from five African countries, as follows (range of detected values, ng/g product): arsenic, 0.064–1.23; cadmium, 0.09–0.65; chromium, 0.68–6.34; nickel, 1.17–4.79; and lead, 0.20–2.81 *(37)*.

8.4 A complex landscape

The market, patterns of use and characteristics of SLT products are not only diverse, as described above, but have also changed (and continue to change) with the introduction of new product categories by multinational tobacco manufacturers.

This section addresses changes in SLT products, marketing and patterns of use and the potential public health implications.

While SLT are used in over 140 countries *(40)*, the prevalence and patterns of use differ widely. Over 359 million people over 15 years of age use SLT, most of whom live in the WHO South-East Asia Region, where there are an estimated 288 million ST users *(1)*. While cigarette smoking is decreasing in most countries, SLT use is increasing, particularly in countries that already have extensive use of SLT . Since 2000, SLT use has increased (independently and as a proportion of total tobacco use) in Bangladesh, India and Nepal; the proportion of SLT of total tobacco use is 61% in India and 41% in Nepal *(41)*. Additionally, the prevalence of dual use of both cigarettes and SLT was 16–23% among tobacco users in Bangladesh, India and Nepal. In some countries, SLT use is considered more socially acceptable among women than men, and use may therefore be more prevalent among women. For example, in Burkina Faso, most tobacco use by men (80%) is in the form of cigarettes, while that by women is almost exclusively SLT *(42)*. Countries in which the current prevalence of SLT use is higher in women than in men are: Bangladesh, Barbados, Cambodia, Cabo Verde, Mauritania, South Africa, Thailand and Viet Nam *(14)*. In many countries, women continue to use SLT such as *gutkha*, *pan masala* and tobacco toothpaste during pregnancy. SLT use is also prevalent in the Eastern Mediterranean Region, with an estimated 23 million adult users, the Western Pacific Region, with an estimated 20 million adult users, the African Region with an estimated 11 million adult users, and the Region of the Americas, with an estimated 8 million SLT users *(1)*. Surveys of SLT use have been conducted in the Bolivarian Republic of Venezuela, Canada, Colombia, the Dominican Republic and the USA, with a prevalence as high as 33.4% in Venezuela *(43)*. In the USA, the prevalence of SLT use among adults is about 2% (4% among men), although it is higher in some groups, such as rural white males and South Asian Americans *(44)*. SLT use is lower in most of Europe (1.1%) but much higher in Sweden (12.3%; 20.7% in men; 3.5% in women) *(45)*.

SLT use is prevalent among youth. Globally, among adolescents aged 13–15 years, it is estimated to be 3.4% (4.0% for boys and 2.8% for girls) *(1)*. Use among youth is particularly high in the African and South-East Asia regions, both estimated at 4.2%. In the WHO African Region, however, only 47% of the population aged 13–15 years were surveyed, so that the results are indicative only; additional surveys may indicate a substantially different average prevalence *(1)*. In the island nations in the Western Pacific Region, the prevalence of SLT use among youth aged 13–15 years is also high, including in the Federated States of Micronesia (16.0%) *(46)*, Marshall Islands (15.2%) *(47)*, Solomon Islands (13.0%) *(48)* and Papua New Guinea (12.2%) *(49)*.

Four key product characteristics have increased the attractiveness of SLT and contributed to the changing market for these products: product formulation, nicotine content, availability and flavourings. New product formulations, such

as portioned moist snuff pouches in Sweden and the USA during the 1970s and 1980s, were developed for easier use, to avoid spitting and to appeal to novice users. Similarly, in India, *gutka*, an industrially manufactured mixture of tobacco, areca nut, slaked lime and flavouring agents, was introduced in the 1970s and sold in single-use sachets. The product was designed for convenience and was heavily marketed to adolescents. With such changes in product characteristics, new strategies for marketing and promotion were developed.

8.4.1 Case studies of product marketing

Moist snuff (Sweden and USA)

In the 1970s, as public awareness of the hazards of smoking grew, a grassroots movement emerged to advocate for restrictions on smoking in shared spaces. SLT product manufacturers saw an opportunity to market their products as an alternative to cigarette smoking. The US Smokeless Tobacco company (later acquired by Altria) embarked on a national marketing campaign to broaden the appeal of what was at the time a niche product, used in rural areas and by workers in factories and other settings where smoking was prohibited. The new marketing campaign featured major sports figures, television and magazine advertisements and product sampling at sporting events, to link SLT use to athletic performance. The US Smokeless Tobacco company even became an "official sponsor" of the 1980 Winter Olympic Games in Lake Placid, NY *(50)*. In the 1980s, the company introduced Skoal Bandits, a low-pH, low-nicotine product, to appeal to new users and to allow them gradually to develop tolerance to nicotine before moving on to higher-nicotine products, such as "Copenhagen" *(51)*. As seen in internal industry documents, the tobacco industry discussed this graduation strategy for introducing new users to SLT and transitioning them to more addictive products *(52)*. Skoal Bandits were aggressively marketed with tactics to appeal to youth, including sports sponsorship, a free sampling programme for university students and stressing that the products could be used in smoke-free offices, bars and other smoke-free spaces *(53)*. As the increase in cigarette sales slowed, sales of moist snuff increased steadily during the late 1970s and 1980s.

Commercialization of gutka in India

As highlighted in the "Smokeless tobacco and public health in India" report *(54)*, in India, the gutka industry has promoted a packaged, ready-to-use version of a traditional custom-made mixture that is portable and easy to use. SLT is a multimillion-dollar industry in India, where there are over 400 brands *(55)*. In the 1980s, with introduction of low-priced, single-portion pouch, sales of gutka and pan masala with tobacco increased substantially as new manufacturers entered the market. While the Cigarettes and Other Tobacco Products Act 2003 *(56)* prohibited tobacco advertising in all media, manufacturers produced brands of pan masala

without tobacco, with brand names the same as or similar to those of tobacco products. Television news channels began including news breaks sponsored by a pan masala manufacturer. Popular celebrities who are appealing to young people have appeared in gutka advertisements. Packets of chewing tobacco were given away for free with areca nut mixtures without tobacco. Brand names and imagery on areca nut products were often aimed at children and women. While packaged gutka products have been banned in India, manufacturers have evaded regulations by separating tobacco from the other ingredients (flavoured areca nut) to be sold in separate packages, although with similar branding, for the user to mix.

SLT products with multinational cigarette brands

Since 2001, a number of manufacturers have introduced SLT products that differ in numerous ways from traditional products and are oriented towards a broader consumer base. The products are formulated differently (e.g. with reduced nitrosamines, in dissolvable form, spitless) and marketed differently from conventional SLT products (on new markets, targeted to current smokers, in innovative packaging). Companies that predominantly marketed cigarettes have entered the SLT market, adding attractive flavourings, such as mint and fruit, and new delivery methods, such as lozenges or small pouches, which eliminate spitting. Major multinational cigarette companies have drawn up sophisticated demographic profiles of SLT users to tailor their marketing for their new products. Subsequently, they introduced snus products carrying the well-known Marlboro and Camel brand names, thereby adding new product lines and using their marketing expertise and brand recognition to advertise this new class of products *(57)*. The tobacco market onto which these newer products are being launched has changed to a certain extent because of the success of tobacco control activities that focused largely on smoking, such as smoke-free environments, high cigarette taxes and increased awareness of the health effects of tobacco use. Some tobacco companies have responded to the tremendous growth of indoor smoke-free laws by advertising SLT products to smokers as temporary alternatives to cigarettes in situations in which they cannot smoke.

8.4.2 Health impact and cessation

Impact on youth and young adults

Potential increases in initiation of SLT use among youth is a major ongoing public health challenge. The increase may be due to the marketing and introduction of new, flavoured products. Thus, SLT use by adolescents and young adults in the USA increased substantially during the 1970s, after introduction of products that were more accessible to new users. Youth who are curious about SLT also tend to be curious about cigarettes and other tobacco products. Exposure to tobacco company communications and advertising is also associated with SLT use, as for cigarettes *(58)*.

New marketing approaches for these products have contributed to increased use among youth, including in Sweden and the USA. Marketing messages can emphasize desirable design features, flavourings, ease of use and nicotine delivery, potentially increasing the attractiveness of the products. Product marketing in the 2000s sought to extend beyond the established SLT user groups to attract more upscale, urban and female users. While initial efforts to extend the market were not successful, because of the strong association between moist snuff products and rural male users, introduction of nicotine pouches and "white snus" products (which are not discussed in this paper) provided a further opportunity to attract new groups of users *(59)*. Free samples and tiered pricing are further strategies used to market SLT products to new users. Adolescents and young adults are sensitive to price, for SLT as well as for smoked tobacco products, indicating that price can influence SLT uptake *(60)*.

Education and media campaigns to prevent SLT uptake and use by youth have not been as widespread as for cigarettes, although there are some examples. The "Real Cost" campaign of the US FDA was designed to educate rural youth about the dangers of SLT use. A longitudinal randomized controlled trial of media markets found that the campaign influenced beliefs and attitudes about SLT among older boys targeted by the campaign *(61)*. While the long-term impact on uptake and use of SLT remains uncertain, the study suggests that a targeted campaign focused on the health consequences of SLT use can influence beliefs and attitudes, which may, in turn, impact SLT use. Anti-tobacco campaigns designed for youth in India address use of both SLT and other tobacco products. A project for Mobilizing Youth for Tobacco-related Initiatives tested a culturally relevant tobacco prevention programme in 32 urban Indian schools to decrease the susceptibility of sixth- to ninth-grade students to both smoked and SLT use *(62)*. A national television and radio mass media campaign targeted to SLT users in India highlighted the harms of tobacco use and encouraged quitting by telling personal stories. It was found to increase awareness and intentions to quit *(63)*.

Health impact

Depending on the types and concentrations of toxicants in products and how they are processed and manufactured, use of SLT products is associated with a range of adverse health outcomes, including oropharyngeal, oesophageal and pancreatic cancers; potentially malignant oral mucosa disorders; diabetes mellitus; cardiovascular diseases; low birth weight; and preterm births *(3)*. Based on an estimate in 2016, SLT use is estimated to contribute to more than 650 000 deaths globally every year *(64)*. An estimated 480 000 of deaths attributable to SLT use occur annually in the WHO South-East Asia Region, the majority of which (79.9%) occur in India *(2)*. In the INTERHEART study, it was estimated that over 200 000 people died of coronary diseases attributed to SLT use in 2010 *(65)*. A recent study

showed that use of non-cigarette tobacco was associated with higher odds of stroke in West Africa *(66)*. SLT use has also been associated with malnutrition in LMIC *(67)*, and households in low-income settings in which tobacco is used make poorer food choices because of the funds spent on tobacco *(68)*. Tobacco use during pregnancy is associated with increased risks of stillbirth and low birthweight *(20)*.

A working group convened by the IARC Monographs programme classified SLT, betel quid with tobacco, betel quid without tobacco and areca nut as carcinogenic to humans on the basis of the strength of the evidence that they cause cancer of the oral cavity *(17)*. In addition, volume 19 of the IARC handbook on oral cancer prevention *(69,70)* states that cessation of use of areca nut products (including betel quid), with or without tobacco, reduces the risk of oral cancer. More than 40 compounds or agents that have been identified as carcinogens by working groups convened by the IARC have been found in SLT products, including TSNA, other nitrosamines, PAH and aldehydes (as described above). A recent analysis concluded that > 120 000 cases of oral cancer (30%) were attributable to use of SLT and areca nut in 2022 *(71)*. In previous global studies, it was estimated that oral cancers attributable to SLT were the cause of 49 600 deaths and 1.4 million disability-adjusted life years in 2017 *(20)*. SLT use differs widely among populations according to differences in product characteristics, patterns of use and the prevalence of competing exposures, such as alcohol use or exposure to human papillomavirus for oral and oropharyngeal cancers. More than 50% of oral cancers in India and Sudan were attributable to SLT, as compared with about 4% in men in the USA *(72)*.

While many studies have shown adverse outcomes in SLT users, including an increased prevalence of oral cancers, the magnitude of the health risks directly associated with SLT use appears to differ by country and region, which may be due to differences among products and use patterns. As discussed earlier, laboratory analyses have shown widely different levels of known carcinogens, additives and nicotine in SLT products in different regions, and epidemiological studies in different regions have estimated various risks for cancer and cardiovascular disease. Few data are available for precise quantification of such differences and for identifying the factors responsible. The overall public health impact of SLT use, apart from their known biological effects, depends on various health and environmental factors, including the prevalence and patterns of use of different products, the impact of marketing messages and the effectiveness of prevention and cessation. As the product market continues to change, the disease risks may also change.

In the IARC handbook on oral cancer prevention *(69)*, the working group concluded that there is sufficient evidence that behavioural interventions in adults are effective in promoting quitting of SLT use. The evidence for pharmacological interventions (alone or combined with behavioural interventions) is still emerging

(69). Similar conclusions were reached in a recent systematic review, which reported substantial efficacy of behavioural interventions for cessation and limited evidence of the efficacy of varenicline and nicotine lozenges *(73)*. A recently updated Cochrane review also showed that higher rates of SLT abstinence are achieved with behavioural interventions than with minimal support and with brief advice than with no support. Varenicline and nicotine replacement therapy are likely to improve SLT quit rates, although the evidence is of low certainty *(74)*. Most of the evidence to date is for high-income countries; however, studies are under way in LMICs with extensive SLT use.

8.5 Regulation and future considerations

8.5.1 Regulatory challenges

SLT poses substantial challenges to regulation because of the wide variety of products, production methods and modes of use. Regulation is particularly complex for products that are not standardized because they are manufactured in local cottage industries or mixed for customers by street vendors at points of sale. Previous WHO TobReg reports have highlighted challenges to the regulation of SLT products because of product diversity *(5)*. Common regulatory challenges for SLT products, some of which were noted previously, are listed below.

- **Product diversity.** A wide range of SLT products with different characteristics and additives is used around the world, including chewing tobacco, snuff, *gutka*, betel quid with tobacco, *snus*, *toombak*, *iqmik* and tobacco lozenges. Such diversity makes it difficult to draw general scientific conclusions about the products as a class.
- **National regulatory capacity.** The ways in which SLT products are produced, sold, used and regulated differ widely among countries. In general, high-income countries have more established regulations and monitoring. In LMIC, a large share of the SLT market remains unregulated.
- **New SLT products that are designed to be appealing**. The tobacco industry has introduced a new generation of SLT products specifically designed to attract a broad group of consumers by the addition of attractive flavourings such as mint and fruit and new delivery methods, such as lozenges or small pouches, which eliminate spitting, making the products more attractive.
- **Lack of standardized terminology**. The terms used to describe SLT in policy or research are not standardized. It would be important to agree on common outcome measures (e.g. adverse health outcomes

and prevalence of SLT use) to record, report and assess the impact of SLT policies and to monitor the SLT epidemic in all countries.

- **Measurement of the impact of policies**. Capacity to assess the impact of policy decisions for SLT may be more limited than for other forms of tobacco.
- **Limited facilities for laboratory testing**. Limited capacity for testing SLT products in countries and regions is another challenge for monitoring and enforcing products regulations.

8.5.2 Regulatory landscape

The WHO FCTC is a landmark global treaty for combatting use of all forms of tobacco. To date, however, countries' regulatory measures have focused more on smoked tobacco than SLT. Comprehensive implementation of the WHO FCTC to regulate all tobacco products, including SLT, is critical to reduce the mortality and morbidity due to tobacco use. Countries have implemented policy measures recommended by the WHO FCTC, including complete or partial bans on sales of SLT, policies related to their environmental and other impact and bans on SLT marketing at sports venues. Requirements for manufacturer reporting and policies on tobacco-free public places, for example, differ by country. Most countries in which SLT are used have policies for all tobacco products, including SLT. Specific policies for SLT, detailed below, are available in at least 61 countries, although the scope of such policies and their implementation may be limited. Of those countries, 16 are in the WHO Region of the Americas, 11 are in the South-East Asia Region, 10 are in the WHO Eastern Mediterranean Region, 9 are in the WHO African Region, 8 are in the WHO Western Pacific Region, and 7 are in the WHO European Region *(12)*.

Taxation and pricing of at least some SLT products have been reported by 16 countries (Algeria, Andorra, Bangladesh, Bhutan, Canada, Hungary, Iceland, India, Japan, Madagascar, Maldives, Norway, Panama, Russian Federation, South Africa and Switzerland) *(14)*. The amount and type of taxation of SLT products differs, however, from country to country and within countries. Unfortunately, the taxes imposed on SLT products are reported to be lower than those on smoked products in many countries *(75)*, which could result in an increase in the prevalence of SLT use *(76)*. A number of countries have explicit regulations for SLT, including Bangladesh, Brazil, Canada, Ecuador, India, Malaysia, United Kingdom, USA and Uruguay *(12)*. The measures range from requiring licensing for selling SLT products (Bangladesh), a ban on additives (Canada), mandatory depiction of ingredients (tar and nicotine contents) on tobacco packs (India, United Kingdom and USA) to prohibition of representation or graphics suggesting the grading, quality or supremacy of the product (Malaysia) *(12)*. The European Union Tobacco

Products Directive (2014/40/EU) mandates the tobacco industry to report the ingredients used in all tobacco products, including SLT products *(77)*.

For the 2025 WHO report on the global tobacco epidemic *(14)*, which reports the progress of tobacco control globally monitoring the most impactful tobacco demand reduction measures, including on warnings of the harms of tobacco, 119 countries reported implementation of either graphic (54 countries) or textual (65 countries) warning labels on product packaging. Pictorial health warnings differ in size, as follows: covering ≥ 50% (Argentina, Bangladesh, Chile, Costa Rica, Egypt, El Salvador, Honduras, Indonesia, Kuwait, Seychelles, Trinidad and Tobago, United Arab Emirates and Viet Nam); 60% front and back (Burkina Faso, Ecuador and Guyana); 75% of the two principal display surfaces (Myanmar); 85% of the principal display areas (India); and ≥ 90% of the principal display areas (Benin, Maldives, Nepal and Timor-Leste). In Brazil, graphic health warnings are required on 30% of the front and 100% of the back of the package. Countries including Australia, Saudi Arabia, Thailand and Uruguay require plain packaging of tobacco products, including SLT. The EU Tobacco Products Directive mandates health warnings on tobacco and related products by all member states *(77)*.

Comprehensive bans on tobacco advertising, promotion and sponsorship are in place in 68 countries, including the members of the European Union through the Tobacco Products Directive *(77)*. In many countries, however, especially LMIC, only partial bans on tobacco advertising, promotion and sponsorship are required, allowing the tobacco industry to directly or indirectly advertise and promote its tobacco products, including SLT products, in many media *(14)*.

The sale of SLT products to and by minors is restricted in many countries; however, such laws are often poorly implemented, especially in countries such as Bangladesh, India, Myanmar and Pakistan, to name a few. Effective tracking and tracing to combat illicit trade in SLT products are not available in most LMICs *(78)*.

Many countries implement policies that are more restrictive than WHO FCTC provisions to curb the negative public health impact of SLT use. SLT were completely banned in at least 23 countries as of December 2024, including the Democratic People's Republic of Korea, Gambia, Mauritius, Singapore, Sri Lanka, Thailand and Uganda *(14)*. Australia, Bahrain, Brazil, all the member states of the European Union (except snus in Sweden), India, the Islamic Republic of Iran, New Zealand, the United Republic of Tanzania and the United Kingdom have imposed partial bans on importing and selling some forms of SLT products *(79)*. Implementation of such bans may, however, be weak, especially in LMICs, and may not be monitored strictly. India prohibits use of plastic sachets for packaging SLT *(80)*. Policies in Canada (requirement for manufacturer reporting) and Guam (tobacco-free policy for all government facilities) also extend beyond WHO FCTC provisions *(80)*.

Article 8 of the WHO FCTC calls for protection of people from exposure to tobacco smoke by prohibiting smoking in indoor public space and workplaces. A number of jurisdictions have gone further; for example, Nepal bans all forms of

tobacco use in public spaces. Such restrictions may also be applied at local level or in particular sectors, such as at sporting venues, particularly baseball stadiums, as observed in Boston, Chicago, Los Angeles, New York and San Francisco in the USA *(81)*. Concern has been raised about potential transmission of infection during spitting after use of SLT. The city of Ahmedabad in India closed shops selling *paan* and other SLT products in 2020, during the coronavirus disease 2019 pandemic to control the spread of infection *(82)*. Limited data are available, however, on the burden of infections attributable to SLT use *(83)*.

Effective tobacco control is possible in rural areas, as exemplified by a community-led tobacco-free village programme in India *(84)*. Nearly 38% of adults in rural India use some form of tobacco, especially smokeless products. A programme was initiated by the Salaam Mumbai Foundation in India, in which villages were engaged, with community education and training of community health workers to implement the programme. Indicators of success included community ownership of the programme, guidance, motivated, committed local leaders, collaboration with grassroots organizations, rewards and sanctions to establish new social norms, and provision of other income-generating options for vendors of tobacco. While the programme required time and dedicated effort and was not successful in all villages, it holds promise for achieving the goals of tobacco control policies, including for SLT, especially in resource-scarce settings *(85)*.

The evidence suggests that taxation and multifaceted policy initiatives, including bans on sales of these products, if effectively implemented and regularly monitored, result in meaningful reductions in SLT use. Changing trends in the use of SLT products emphasize the importance of comprehensive programmes to address use of these products. Intervention strategies must be adapted to the local context, rates of tobacco use and trends in consumption of tobacco products, including SLT.

8.5.3 Examples of studies on regulation of SLT

Use of food laws by Indian states to ban certain SLT products

SLT are used more widely than smoked tobacco in India. SLT are used by 21.4% (199.4 million) adults *(86)*, and 10.7% (99.5 million) use smoked tobacco products. The extensive use of SLT products has contributed to the increasing incidences of oral submucous fibrosis and oral cancer in the country, especially among younger groups. In India, notifications under the food laws – the Prevention of Food Adulteration Act 1954 (PFA) *(87)* and, later, the Food Safety and Standards Act 2006 (FSSA) *(88)* that replaced the former law – prohibit use of tobacco and nicotine in food products. Although the two laws were enacted by the national government, they were strategically administered by Indian states in the interest of public health. The tobacco industry challenged these regulations in court, arguing that *gutka* and *pan masala* are not food products and hence cannot be regulated

by food laws. While the notification banning chewing tobacco products under the PFA was evoked on the grounds that only the national government had the power to ban a product under the PFA, the notifications issued under the FSSA continue to enable stricter regulations. Despite challenges from the tobacco industry, most Indian states and union territories have successfully used the food laws to issue orders prohibiting the manufacture and sale of certain SLT products, especially *gutka*, in their jurisdictions *(79)*.

SLT regulation in Bangladesh

Despite the high prevalence of SLT use in Bangladesh, SLT was not included in the Tobacco Control Law until 2013. Subsequently, the Smoking and Tobacco Product Usage (Control) (Amendment) Law, 2013 Section 2 (C) *(89)* covered SLT, including *gul*, *zarda*, *khoinee* and *sadapata*, in the definition of tobacco products. Accordingly, relevant sections of the law became applicable to SLT, including the ban on tobacco advertising, promotion and sponsorship, sale of tobacco products to and by minors, graphic health warnings on packs of tobacco products and disclosure of the content of imported tobacco products. In case of a violation, an authorized officer may prosecute the perpetrator in a court of law, which may impose the relevant penalty. As use of SLT is culturally accepted in Bangladesh, however, appropriate public awareness campaigns are necessary to curb SLT use, with increased taxes on these products and provision of high-quality, population-based cessation services.

Use of SLT products banned in public places in Nepal

SLT use is a major public health concern in Nepal. The Tobacco Product (Control and Regulation) Act, 2010 *(90)* bans use of all tobacco products, including SLT, in public places, including Government offices, educational institutions, public vehicles, libraries, health posts, airports, old-age homes, orphanages, public toilets, cinema halls and theatres. The Act also prohibits the sale of SLT to children < 18 years of age and pregnant women, and the promotion, advertisement and sponsorship of these products. Additionally, SLT packages must have graphic health warnings covering 90% of the principal display areas.

8.5.4 Opportunities and considerations for the future

Most global tobacco control programmes have addressed prevention and control of cigarette smoking, with little or no focus on SLT, despite evidence that tobacco control policies and interventions for SLT can be effective. In many regions, even where SLT use is highly prevalent, policies and programmes for prevention and cessation are generally weaker than those that address smoked tobacco. Prices are lower, warning labels are weaker, surveillance is less developed, fewer proven interventions are available, and fewer resources are devoted to control. But SLT

use is no longer a localized or regional issue; it is a major challenge for a large percentage of the world's population *(1,3)*.

SLT are difficult to regulate because of the wide variety of products and production methods, such as those manufactured in local cottage industries, comprising an estimated 91.3% by volume of SLT products worldwide *(3)*. These products, widely used in countries such as Bangladesh and India, are assembled by local vendors and often tailored to the customer's preferences. As documented in previous WHO TobReg reports *(4,91)*, the ingredients and other characteristics, such as the levels of nicotine and other toxic and carcinogenic constituents, vary widely from one sample to another. SLT products often contain ingredients other than tobacco, such as areca nut and flavourings, which can increase the health risks.

Regulations to change the marketing strategies of the tobacco industry may affect the future public health impact of SLT. In some high-income countries in which restrictions on public smoking have increased and smoking prevalence has decreased, tobacco companies have marketed SLT products to smokers. The impact of this trend on smoking behaviour and dual or poly-tobacco use remains uncertain. Furthermore, both smoked and smokeless products of multinational tobacco companies are increasingly present in LMIC.

SLT use presents a threat to health equity, as it tends to be highest among lower-income populations *(1)*. SLT is culturally acceptable in much of the WHO South-East Asia Region, where its use, alone or with areca nut in betel quids, has resulted in one of the highest incidence rates of head-and-neck cancers (mainly mouth and tongue) in the world. Moreover, the levels of toxic constituents tend to be higher in products used in India and other high-burden countries *(13)*.

Fewer data are available on SLT products and patterns of use than for cigarettes. Global data sources for tracking SLT use include the Global Adult and Youth Tobacco Surveys, the WHO STEPwise Approach to NCD Risk Factor Surveillance surveys, Global School-based Student Health Surveys, Demographic and Health Surveys and national health surveys. Administration of such surveys, however, requires substantial resources, and they are conducted only intermittently in most countries. Thus, many countries have no recent surveillance data on SLT use.

In previous WHO TobReg reports, studies on SLT have been reviewed and recommendations made to advance regulation and control of SLT. In particular, the fifth *(4)* and sixth *(5)* reports include recommendations for applying WHO FCTC measures to SLT, product regulation to reduce product toxicity and use of standardized measures and protocols. The recommendations in the two reports include the following.

- The public health challenge of SLT warrants far greater attention and action than it has received so far in view of the extent and complexity of the problem, marketing, trends in patterns of use and lack of effective treatment.

- Tobacco control policies, programmes and interventions applied to cigarettes and smoked tobacco products should also be applied, enforced and monitored, with equal rigor, to SLT products, particularly in regions where the prevalence of use is high. This includes ensuring that implementation of WHO FCTC measures includes SLT.
- Prevention and cessation of SLT use should be an integral part of a comprehensive tobacco control programme.
- No intervention strategy will apply to all countries. Approaches must be tailored to the social context, product type and prevalence and trends in consumption of all tobacco products.
- Given the wide variation in levels of toxicants in different types of SLT products, requirements should be introduced to limit toxicity, including: reducing the use of *N. rustica* tobacco, limiting bacterial contamination, requiring that tobacco be flue- or sun-cured rather than fire- or air-cured, killing bacteria by pasteurization, improving storage conditions such as refrigerating products before sale, affixing the date of manufacture and eliminating other toxic ingredients such as areca nut.
- Upper limits on toxicants should be mandated for SLT products manufactured by industry, with an upper limit for NNN and NNK of 2 µg/g of dry tobacco and an upper limit for benzo[*a*]pyrene of 5 ng/g.
- Steps to reduce the appeal of and addiction to tobacco products should include banning or regulating sweeteners and flavourings (including herbs, spices and flowers) and setting limits on free nicotine and pH.

The following sections extend these and previous TobReg statements to highlight remaining research gaps and propose additional policy recommendations.

8.6 Research gaps, priorities and questions

Several areas of research on SLT warrant attention to ensure information for future control and regulation, including further characterization of diverse products and ingredients, better understanding of the health effects associated with different product types and practices, adaptation of evidence-based control measures to address smoking and novel interventions to treat dependence in SLT users. SLT products have serious adverse health effects, although the risks associated with different products and regions are unknown, which is an important research area for further characterization. Previous WHO TobReg reports (*4–6)* have highlighted the need for further research to evaluate exposure to nicotine and toxicants in SLT, the associated health risks and the effects on population health of changing patterns of use. They also recommended extending laboratory capacity

through regional hubs and cooperation in developing standardized methods and measures for research *(5)*.

Additional priority research gaps are as follows.

- More data are required on the toxicity and addictiveness of the diverse new SLT products. International data on these products, their contents and their toxicant levels will be critical for governments to regulate them effectively.
- Further standard testing methods should be developed to set limits on the permitted levels of toxicants in SLT products. Coordinated regional testing will ensure that the characteristics of SLT products in different countries and regions are recognized. Coordinated testing would be useful for countries with limited capacity and funding for independent testing.
- Effective interventions for cessation of SLT use are available. WHO recommends behavioural interventions, varenicline or nicotine replacement therapy for SLT users who wish to quit. Such strategies, however, should be further tailored and evaluated. Access to such interventions, especially by young people, and methods for assessing their impact and sustainability are necessary.
- More information is necessary about SLT use behaviour, such as dual use of smoked and SLT products, and its impact on quitting intentions, quitting behaviour and initiation of use.
- Further quantification of the risks associated with SLT use will be important for setting policies to reduce the burdens on health, the effects on national economies and the environment and the social costs of increasing SLT use by young people. Little study or documentation is available on the costs of SLT use or on the effects on health care and economies. Tools for collecting information for surveys should be adapted to provide more information on use of SLT.
- As SLT pose a challenge to health equity, further research should be conducted on disparities in SLT use and the related health effects. In particular, studies should be conducted of low-income and vulnerable groups in high-burden countries to better understand the factors that influence SLT use, including cultural and psychosocial factors. For example, studies of the relation between SLT use and household nutrition and economics could enrich studies of the relation between SLT use and poverty.

8.7 Policy recommendations

As noted in previous TobReg reports, the measures called for by the WHO FCTC for effective tobacco control should be fully implemented in letter and in spirit by all Parties by recognizing control of SLT use as important as control of use of cigarettes and other tobacco products. Tobacco control policies and programmes should be reviewed to identify opportunities and gaps to address SLT. Effective implementation of the WHO FCTC for SLT requires adaptation and tailoring of policies and interventions to address SLT. Especially in LMICs, social, cultural and economic factors are central to SLT use, and perception of health risks and should be accounted for in the design and implementation of SLT policies and interventions *(8)*. Recommendations further to those already made by TobReg are provided below.

- **Monitoring and surveillance.** Extended monitoring and surveillance are necessary to further characterize SLT use globally and to track how changes in the marketplace and in tobacco control affect patterns of use. Monitoring should include laboratory studies of product characteristics and constituents, tracking of product packaging and marketing and surveys of SLT use and health effects in adults and youth. Standard terminology should be developed to describe the various SLT products and their characteristics in various settings.
- **Building research and testing capacity for effective regulation of SLT.** Greater capacity is necessary for research and testing on product regulation. The fifth WHO TobReg report *(4)* noted the importance of capacity-building and collaborative networks so that countries could share information and skills and develop "best practices" for product analysis and regulation. Resources and networks coordinated by WHO, such as the technical advisory groups of WHO, TobReg and TobLabNet, provide a platform for building capacity and collaboration.
- **Building country capacity to identify and counter illicit trade of SLT.** Global tobacco control partners should help countries to identify counterfeit SLT products, in addition to counterfeit cigarettes. Country and regional cooperation are essential to support testing of SLT and to counter the challenge of illicit trade. Countries are encouraged to ratify the WHO FCTC Protocol to Eliminate Illicit Trade in Tobacco Products *(92)*.
- **Wide dissemination of information and evidence on SLT use.** Information and evidence about SLT use should be disseminated to policy-makers, researchers, professionals and other stakeholders to establish programmes to combat SLT use and its effects. Civil society and the public could play important roles in generating international awareness of the hazards of SLT use in relevant grass-roots forums.

- **Fully tobacco-free spaces**. Policies governing tobacco use in public spaces have been addressed primarily to cigarettes and other smoked tobacco products. Some local policies, however, have extended such restrictions to SLT use. While the risk of use of SLT for people nearby is not the same as that of second-hand smoke, some SLT products require spitting, which can transmit disease. The creation of tobacco-free workplaces and public spaces benefits health by encouraging cessation and promoting a culture free from tobacco use. Thus, restricting SLT use in public spaces is an important step in the ongoing denormalization of tobacco use.
- **Bans on classes of SLT products.** Such bans have been adopted as a viable regulatory option by many countries *(3),* such as European Union that ban snus and India that ban packaged gutka; however, such measures are difficult to implement without sufficient administrative capacity, clear definitions of SLT products and a comprehensive tobacco control strategy. It may be difficult to enforce a ban on SLT in only one country, in view of the trend to elimination of non-tariff barriers to trade among countries *(77)*. Once a product ban is fully enforced, regularly monitored, in a comprehensive tobacco control programme that includes measures to combat illicit trade in SLT, treatment for tobacco dependence and education on the dangers of using SLT, it can further motivate and enable SLT users to quit.
- **Preventing uptake and reducing tobacco use among adolescents and young adults**. SLT use tends to be higher among youth in some areas, and tobacco use of all forms tends to begin during youth. The tobacco industry has specifically targeted youth with products and marketing strategies designed to appeal to novice users. Policies and interventions to reduce youth uptake and use include strict age restriction, banning the use of flavours to make them less attractive and appealing, comprehensive bans on tobacco advertising, promotion and sponsorship, including on the Internet and social media, increased taxes and restricting youth access and exposure to products, advertising and displays at points of sale.
- **Large graphic health warnings and standardized packaging.** Standardized packaging addresses the challenges of effective enforcement of packaging regulations for SLT products, which are often in small, irregular packages or no packaging and are often manufactured by small local producers. Large graphic health warnings and standardized packaging of SLT products should nevertheless be required and enforced to warn about the dangers of the products.

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9. Tobacco and nicotine product characteristics and relevant standards

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Contents

Abstract
9.1 Background
9.2 Methods
9.3 How manufacturers carefully design tobacco and nicotine products to influence their attractiveness, addictiveness and toxicity
9.3.1 Attractiveness
9.3.1.1 Flavours
9.3.1.2 Additives that reduce harshness and contribute to flavour
9.3.1.3 Ingredients added to imply health benefits or stimulating effects
9.3.1.4 Cigarette filters and filter ventilation
9.3.1.5 Product dimensions (not including packaging)
9.3.1.6 Attractive design features (not including packaging)
9.3.2 Addictiveness
9.3.2.1 Total nicotine content as a function of tobacco type
9.3.2.2 Total nicotine content as a function of product unit size
9.3.2.3 Product characteristics that alter nicotine bioavailability in cigarette smoke
9.3.2.4 Unprotonated nicotine in smokeless tobacco products
9.3.2.5 Nicotine forms in ENDS and nicotine pouches
9.3.3 Toxicity
9.3.3.1 Tobacco type
9.3.3.2 Additives, including menthol
9.3.3.3 Product dimensions
9.3.3.4 Cigarette filters
9.3.3.5 Filter ventilation
9.3.3.6 ENDS device characteristics
9.3.4 Careful balancing of product design features by manufacturers
9.4 Product standards and how can they be used to reduce use of tobacco and nicotine products
9.4.1 Use of product standards to reduce demand for tobacco and nicotine
9.4.1.1 Product standards to reduce the attractiveness of tobacco and nicotine products
9.4.1.2 Product standards to reduce potential dependence and addiction to tobacco and nicotine products
9.4.1.3 Product standards to reduce the toxicity of tobacco and nicotine products
9.5 Industry tactics
9.5.1 Circumvention of flavour bans
9.5.2 Circumvention of regulation of nicotine products and/or nicotine standards
9.6 Impact and measurement of the effectiveness of product standards
9.7 Policy recommendations
References

Abstract

Tobacco and nicotine product characteristics are carefully designed by manufacturers to maximize the sensory appeal and the elasticity (i.e. users' ability to achieve their desired nicotine intake) of products. This paper reviews the key product characteristics that contribute to the addictiveness, attractiveness and toxicity of tobacco and nicotine products and the potential impact of relevant product standards. Product standards to target the attractiveness and addictiveness of products, such as banning flavours and other additives, reducing nicotine content and banning decorative and other design elements that make products appealing to children, young people and other users, are likely to reduce the prevalence of product use. Such measures may also reduce harmful exposures during tobacco and nicotine product use by reducing the intensity and/or amount of product use. The paper provides examples of some regulatory measures that address product characteristics and industry tactics in response to such regulations. It also proposes research directions and recommends policies.

Keywords: Product characteristic, product standard, attractiveness, addictiveness, toxicity, tobacco, nicotine

9.1 Background

Tobacco and nicotine products, including smokeless products, are carefully designed by manufacturers to maximize product appeal to users. A key focus of product design is effective delivery of nicotine, a powerfully addictive chemical and the main reason for use of tobacco and nicotine products. In addition, certain product characteristics affect the chemosensory experiences of users and/or reinforce misperceptions about product harm. Such characteristics include cigarette filter ventilation, which is associated with perceptions of reduced harm; various additives that reduce the inherent harshness of nicotine in cigarette smoke or electronic cigarette aerosols; flavouring agents, which make products more appealing to both naive and experienced users; and descriptors on product packaging that imply reduced risks or enhanced pleasure from use. In each tobacco or nicotine product, various characteristics act in interconnected and complementary ways to define the addictiveness and attractiveness of the product. Many such characteristics also have a strong impact on product toxicity, defined here as the toxic and carcinogenic effects of the product in users, due to both the chemical composition and the delivery of contents and emissions to users.

Articles 9 and 10 of the WHO FCTC address testing and measurement of the contents and emissions of tobacco products, their regulation and disclosure of information on contents and emissions to governmental authorities and the

public. The partial guidelines for implementation of Articles 9 and 10 of the WHO FCTC *(1)* outline measures to assist Parties in strengthening their tobacco-control policies through regulation of tobacco products and disclosures. The regulation may involve setting limits on nicotine and other key constituents in tobacco product contents and emissions, prohibiting certain additives or standards for product design features and packaging, such as limiting cigarette length and diameter, standardizing colours (e.g. of cigarette paper or filters) or banning descriptors. Such standards contribute to reducing the addictiveness, attractiveness and toxicity of tobacco products and are therefore powerful tools for decreasing the morbidity and mortality attributable to use of these products.

This paper provides an overview of key characteristics responsible for the addictiveness, attractiveness and toxicity of tobacco and nicotine products and a summary of research on setting product standards to regulate such characteristics. Although electronic non-nicotine delivery systems are not mentioned, most of the considerations (except for nicotine) are applicable, as those products are usually indistinguishable from electronic nicotine delivery systems (ENDS). The paper does not cover therapeutic nicotine products authorized for nicotine or tobacco cessation, such as nicotine gum, lozenges and patches. It is strongly recommended that, before taking regulatory action, countries carefully consider all the scientific research that may inform it. Examples of country experiences in setting product standards are presented, and the challenges and recommendations are discussed. This paper includes:

- an overview of characteristics that influence the attractiveness, addictiveness and toxicity of tobacco and nicotine products;
- an overview of product standards and how they can reduce the attractiveness, addictiveness and toxicity of tobacco and nicotine products, with country case studies;
- tobacco industry tactics for resisting and circumventing product standards;
- the impact and measurements of the effectiveness of product standards;
- implications of the findings and research directions; and
- policy recommendations.

9.2 Methods

Preparation of this review included consideration of previous technical reports of TobReg that address product characteristics. A literature review was conducted to capture developments in the field over the 7 years since the previous TobReg report on cigarette characteristics *(2)* was prepared. The literature was searched primarily in the PubMed database, and relevant articles cited in the publications identified were also included. Keywords such as "tobacco product characteristics" and

"nicotine product characteristics" and terms referring to product characteristics of interest (e.g. "menthol ban", "cigarette filter ventilation", "nicotine reduction") were used. In addition, an open search of the Internet was conducted to identify websites that provide information on product characteristics and marketing and also the websites of various regulatory agencies and other information relevant to country experience in setting product standards. The search was conducted between January and December 2024. Relevant information on the regulatory status in Member States was updated during the review with the most recent data from the WHO report on the global tobacco epidemic, 2025 *(3)*.

9.3 How manufacturers carefully design tobacco and nicotine products to influence their attractiveness, addictiveness and toxicity

Nicotine delivery and users' sensory experience influence a wide range of tobacco use behaviours, including initiation, progression to nicotine addiction and brand selection or loyalty, in habitual users. For example, a combination of nicotine delivery and sensory cues is key to smoking satisfaction *(4,5)*, psychological reward *(6)*, craving reduction *(7)* and risk perception *(8–10)*. Below are examples of cigarette characteristics that affect sensory cues, nicotine delivery, risk perceptions and toxicity of various tobacco products, including some relevant internal industry research to illustrate how manufacturers carefully design product characteristics to enhance product appeal.

9.3.1 Attractiveness

Product characteristics that influence appeal include flavours, additives that reduce harshness and other unpleasant sensory experiences, attractive design features, product dimensions and ingredients that imply health benefits or stimulating effects.

9.3.1.1 Flavours

As discussed in "Flavours in tobacco and nicotine products: new developments, implications and regulation" in this report and in previous WHO TobReg reports on flavours and in the literature *(11–13)*, addition of flavours to tobacco and nicotine products increases their appeal by enhancing the sensory experience of users, masking the unpleasant taste or "mouth feel" of tobacco or smoke and facilitating misperceptions of reduced toxicity. It is well established that flavoured tobacco products appeal particularly to young adults, adolescents and women, are implicitly and often explicitly marketed to these populations and are more likely to serve as starter products *(14–17)*. Abundant data from research in various countries show a higher prevalence of use of flavoured tobacco products among

younger people, women and individuals who are aware of smoking-related health risks *(14,18)*.

Menthol has long been the most commonly used flavouring additive in conventional tobacco products, such as cigarettes and smokeless tobacco. The cooling effects of menthol have been exploited by manufacturers to mask the harshness of smoke and encourage initiation and continued use of tobacco and nicotine products by certain population subgroups, including youth *(19)*. The flavours used in smoked tobacco products have been extended recently to include a wide variety of fruit, sweet and other flavours in cigars and cigarettes *(20)*. Use of waterpipes is largely predicated on the wide variety of flavours in these products *(21)*. In addition, expansion of the nicotine product market over the past two decades has been accompanied by a significant increase in addition of sweet, fruity, complex or exotic flavour varieties in ENDS, nicotine pouches and other relatively recent additions to the global tobacco product inventory. The availability of a variety of flavours plays an important role in the attractiveness and appeal of such products; for example, flavoured liquids are often cited as a primary reason for ENDS use and are associated with experimenting with or initiating use of these products *(22–24)*.

9.3.1.2 Additives that reduce harshness and contribute to flavour

Nicotine is a weak base and is present in tobacco plants primarily in the protonated salt form. At higher pH, which is often found in manufactured tobacco and nicotine products, nicotine changes to its unprotonated, biologically available form, which quickly penetrates tissues but has a harsh taste *(25–28)*. pH-Dependent harshness is relevant to both inhaled (e.g. cigarettes and ENDS) and oral products (e.g. smokeless tobacco, nicotine pouches). To alleviate the harshness and make products more palatable, manufacturers often use various types of additives to reduce the pH of product contents or emissions. For example, ingredients such as brown sugar, honey, corn syrup and molasses are common additives to cigarette for this purpose *(29,30)*. During cigarette use, sugars decompose, producing acids, which reduce smoke pH and its harshness. Although a reduced pH decreases the amount of nicotine present in the unprotonated (biologically available) form, it allows deeper inhalation because of the reduced harshness, resulting in a net increase in exposure. In addition, thermal decomposition of sugars results in various caramelization and pyrolysis by-products, which provide a smoother, more flavourful smoke. More information on the role of sugars in tobacco and nicotine products is provided in "Science of sugars in tobacco and nicotine products and regulatory recommendations, an update" in this report. Another important additive to cigarette tobacco is the ammonia precursor diammonium phosphate. The ammonia formed from this precursor in situ in cigarettes forms volatile nitrogen compounds during cigarette use, which enhance the flavour and

the sensation of a "full-bodied" taste of the smoke *(31–33)*. Spice flavours such as cloves, cardamom and saffron are added to some smokeless tobacco products.

Most early versions of e-liquids for ENDS had an alkaline pH (> 7) and contained nicotine in the free-base form *(34–36)*. Not surprisingly, the aerosols formed from such liquids are difficult to inhale, resulting in predominantly oral absorption of nicotine, and users tend to select liquids that have a lower nicotine content. Introduction of nicotine salts in the early 2010s, however, and their rapid growth in popularity has led to the proliferation of high-nicotine concentration e-liquids. These liquids have added organic acids, so that nicotine is present in a protonated, easy-to-inhale form, resulting in higher (in some cases, comparable to that in cigarettes) nicotine intake by users *(37,38)*. The type of salt used in an ENDS liquid (e.g. lactic, benzoic, laevulinic) can also affect the aroma of the aerosol, further contributing to the palatability of the product *(39,40)*. Nicotine salts are also used in some nicotine pouches to facilitate the dissolution of nicotine in saliva.

9.3.1.3 Ingredients added to imply health benefits or stimulating effects

Some cigarette brands are manufactured with ingredients (e.g. components of the tobacco blend, including tobacco type) that are added to imply or invoke perceived health benefits, such as organic tobacco and medicinal herbs. Examples include American Spirit cigarettes marketed in the USA and Yuma Organic cigarettes marketed in Spain, both of which contain "organically grown" tobacco. Marketing of these cigarettes misleadingly identifies organic tobacco as a natural, biological product, which is likely to appeal to smokers who are concerned about the health consequences of their smoking but are unwilling or unable to quit. As has been shown for American Spirit cigarettes, however, the levels of toxicants and carcinogens in tobacco and smoke that are most clearly responsible for the diseases caused by tobacco use are no different in the varieties of this brand made with "organic" and with regular tobacco *(41)*. More information on the development of cigarettes that may have implications for cigarette addictiveness, attractiveness and/or toxicity is provided in the paper "Evolving design, additives and accessories for cigarettes and effects on addictiveness, attractiveness and toxicity" in this report.

Cigarettes that contain medicinal herbs or their extracts in addition to tobacco are marketed mainly in Asian countries *(42)*. They are explicitly marketed as less harmful or even therapeutic, with no scientific evidence to support the claims but with the messages that are potentially appealing to some users.

Tobacco and nicotine products, including ENDS, that contain caffeine as an additive are marketed as energy enhancers. While the concentration of caffeine in ENDS liquids is significantly lower than in traditional caffeinated beverages (e.g. coffee) *(43)*, such products may appeal to users who seek alertness, focus and increased energy.

9.3.1.4 Cigarette filters and filter ventilation

Cigarette filters, and later filter ventilation, were introduced by manufacturers after publication of two major journal publications that raised public concern about the health effects of cigarettes, the British Doctors Study in the early 1950s *(44,45)* and later related publications, such as the US Surgeon General's report in 1964 *(46)*. Due primarily to marketing by the tobacco industry, smokers started switching to filtered cigarettes in the 1950s, and more than 90% of smokers currently smoke such cigarettes. Although there has been no overall reduction in disease risks associated with smoking, consumers tend to believe that filtered cigarettes are safer than unfiltered cigarettes *(47)*. Filter ventilation (small holes in cigarette filters) was later introduced by manufacturers to reduce machine-measured yields of toxicants in mainstream smoke and as yet another deceptive tactic to suggest a reduction in risk to smokers. Further, filter ventilation contributes to cigarette attractiveness by changing how a user experiences smoking and perceives its health risks. People who smoke cigarettes with higher filter ventilation report that their cigarettes taste "lighter" than regular cigarettes and mistakenly believe that their exposure to harmful smoke constituents is reduced *(8,9,48)*. Even the banning of descriptors such as "light" and "ultra-light" from cigarette packs did not change such beliefs *(49,50)*. Further information on cigarette filters and their implications are provided in "Cigarette filters: implications for smoking behaviour, health effects and the environment" in this report.

9.3.1.5 Product dimensions (not including packaging)

Like attractive design features, product dimensions are mainly a means for increasing the attractiveness of tobacco cigarettes and, potentially, similar products, such as cigarillos and bidis. For example, there is sufficient evidence that longer, slimmer cigarettes appeal to women and are generally perceived by smokers as stylish, of higher quality and less harmful *(51–54)*. There is also evidence from research on tobacco industry documents that manufacturers use such perceptions in marketing their products to women *(17)*. It should be noted that small, discreet ENDS products may also be appealing to young people because they are easy to conceal.

9.3.1.6 Attractive design features (not including packaging)

Colour and designs on products are also used to increase their attractiveness, which is particularly relevant to tobacco cigarettes, as studies show that different colours and patterns of cigarette filters and paper affect product appeal and the perception of relative harm *(51,53–55)*. For example, filter tips that are white and/or have attractive elements are perceived as more appealing and less harmful, which suggests that white tipping paper on cigarettes with ventilated filters is

designed to reinforce the perception of a safer product, in contrast to most full-flavoured cigarettes, which have cork-coloured filter tips *(54,56)*. Brightly coloured cigarette paper may also have greater appeal and lead to a perception of less harm, while dark colours are likely to have the opposite effect, unless attenuated by a pleasant aroma and slim design *(2)*.

9.3.2 Addictiveness

Nicotine is the primary addictive substance in tobacco and nicotine products, and nicotine delivery (the amount and the pharmacokinetics) is a major determinant of the satisfaction and the continued use by users with established nicotine dependence *(57,58)*. Therefore, nicotine content and the elements that affect its bioavailability are key product characteristics that influence the addictiveness of tobacco and nicotine products. Certain additives that facilitate nicotine intake by reducing harshness also contribute to product addictiveness by allowing higher intake of nicotine.

9.3.2.1 Total nicotine content as a function of tobacco type

Nicotine levels differ by tobacco plant species, cultivar and even by various parts of the same plant (e.g. stalk position of the leaf) *(59,60)*. Therefore, the type of tobacco used in preparation of a tobacco product, blending of different tobaccos and also the proportion of expanded and/or reconstituted forms play key roles in its addictiveness. This is relevant to cigarettes, smokeless tobacco and other products that contain tobacco. For example, while *Nicotiana tabacum* is the most widely used commercial tobacco species, certain smokeless products sold in India and some other South Asian countries contain *N. rustica*, which contains very high levels of nicotine *(61,62)*. Therefore, regulation of tobacco type (e.g. banning use of types that contain high levels of nicotine) could substantially reduce the nicotine content of products to levels that would not increase nicotine intake by compensatory smoking and therefore make products less addictive.

In the case of ENDS liquids and nicotine pouches, the concentration of nicotine is a direct consequence of the product formulation. In addition, nicotine may not be extracted from tobacco but synthesized from non-tobacco starting materials. In this case, tobacco types used would not be a relevant consideration.

9.3.2.2 Total nicotine content as a function of product unit size

The amount of nicotine per single-use unit of tobacco or nicotine product — such as the filler of one cigarette, a single nicotine pouch or an ENDS product — depends on the weight of tobacco or the volume of e-liquid present in the unit. It should be noted, however, that manufacturers may further manipulate the product design to achieve higher nicotine yields, even from smaller products.

For example, super-slim cigarettes may not reduce nicotine delivery and can pose risks of addiction comparable to those of conventional cigarettes, as demonstrated in Canada, where super-slim cigarettes were shown to yield a similar amount of nicotine as other Canadian cigarettes, suggesting that the addictive potential of super-slim and regular cigarettes may be similar *(63)*. In addition, as noted above, many currently marketed nicotine salt-based ENDS products contain much higher concentrations of nicotine than earlier versions, resulting in a higher total nicotine content per similar volume of e-liquid.

9.3.2.3 Product characteristics that alter nicotine bioavailability in cigarette smoke

As mentioned earlier, the pH-dependent proportion of total nicotine that is present in a biologically available unprotonated form determines the rate of nicotine absorption into the user's bloodstream. Therefore, while an alkaline pH of cigarette smoke makes it harsh and difficult to inhale, an acidic pH will result in only a fraction of total nicotine being bioavailable once the smoke is inhaled. Several product characteristics are being used by manufacturers to alter nicotine protonation in cigarette smoke and its effective absorption into the lung, to increase the rate of nicotine delivery to users and thus making products more addictive.

Tobacco type. The pH of the smoke from air-cured tobaccos can be as low as 6.5, while the smoke from a Burley cigarette can have a pH greater than 7.5 *(64)*. Expanded tobacco may be rich in nitrate and release ammonia into the smoke, both contributing to increased pH *(64,65)*.

Cigarette filters. Cigarette filters contribute to the addictiveness of cigarette smoke by reducing the particle size of smoke, which allows a greater fraction of inhaled mainstream smoke to reach the lungs than from unfiltered cigarettes *(66,67)*.

Filter ventilation. Filter ventilation can increase the pH of smoke (and subsequently the amount of unprotonated nicotine) by affecting the tobacco burn rate and smoke particle size *(68–70)*.

Additives. Addition of ammonia and diammonium phosphate to tobacco contributes to its addictiveness by increasing smoke pH and thus the amount of unprotonated nicotine *(71)*.

Certain additives that decrease rather than increase smoke pH, such as sugars, can also contribute to addictiveness by masking the harshness of smoke, making it easier to inhale larger amounts of nicotine. Additives such as cocoa and menthol are potential bronchodilators and can therefore also contribute to addictiveness by facilitating more effective total nicotine absorption *(72)*. Further, products of the thermal degradation of sugars and some of the psychoactive substances present in cocoa may inhibit monoamine oxidase, which could reinforce the actions of nicotine and thereby increase the addictiveness of smoking *(65)*.

Other cigarette characteristics that may alter the delivery of nicotine or other harmful constituents include cigarette circumference, cigarette length, paper porosity, burn rate, filter efficiency, filter pressure drop and tobacco moisture *(73–76)*.

9.3.2.4 Unprotonated nicotine in smokeless tobacco products

Manipulation of product pH is the main means for increasing nicotine bioavailability and the addiction potential of smokeless tobacco. The relations with product pH is more straightforward than for cigarettes, as no burning is involved. Manufacturers produce and market smokeless tobacco varieties with similar amounts of total nicotine but drastically different amounts of unprotonated nicotine because of variability differences in product pH. This is consistent with the previously reported "graduation strategy" used by the industry, in which new users are encouraged to start with lower-pH brands and gradually use brands with increasing nicotine content as they develop addiction, eventually "graduating" to the brand with the highest content of unprotonated nicotine *(77)*. While such a "graduation strategy" is no longer openly advertised, the availability of products with a wide range of pH allows consumers to self-select products along the continuum of unprotonated nicotine content. Therefore, a product standard that would limit smokeless tobacco pH while setting limits on total nicotine content could reduce product addictiveness and the transition of users to more addictive products. Marketing of the US-manufactured Marlboro Snus, which had low levels of total and unprotonated nicotine and was eventually discontinued because of low consumer uptake, suggests that such product standards may reduce the prevalence of smokeless tobacco use.

In India and some other countries, smokeless tobacco products are either pre-mixed or sold with packets containing alkaline (i.e. pH-increasing) agents such as slaked lime and others so that consumers can add such ingredient to the tobacco according to their preferences *(61)*. Banning sales of alkaline ingredients would be an important measure, with a standard for reducing the pH and total nicotine content of a smokeless tobacco product.

9.3.2.5 Nicotine forms in ENDS and nicotine pouches

The shift towards nicotine salt-based e-liquids was a crucial step in the explosion of ENDS popularity, especially among youth *(78)*. By masking the harshness of nicotine, nicotine salts made it easier to inhale ENDS aerosols with high concentrations of nicotine, which were not possible with the earlier versions of ENDS. This also increased nicotine delivery, resulting in development of strong addiction of users to ENDS *(79)*. In addition, salt-based liquids in ENDS not only allow higher levels of nicotine but may be accompanied by more intense flavouring, as shown for products on the Dutch market *(80)*. Therefore, the presence of

nicotine in salt form, the nicotine concentration and the volume of the container are the product characteristics that define the addictive potential of ENDS.

Some nicotine pouches also contain nicotine salts, although there is substantial variation in the nicotine content of different brands, and the pH of the product is generally slightly alkaline (i.e. > 7) *(81)*. The impact of this combination on nicotine delivery and the addictive potential of nicotine pouches is not well understood; however, sales of these products have been increasing dramatically around the world, and there is evidence of an association between the sales volume and the nicotine content of the pouches *(82)*.

9.3.3 Toxicity

Product characteristics that influence toxicity include tobacco type, how it is processed and blended, the presence of certain additives and the dimensions and other physical features of the product. Products that contain an electronic device, such as ENDS and heated tobacco products, are more complex because of the electronic components and settings, which affect the toxicity of the emissions generated during use.

9.3.3.1 Tobacco type

Manufacturers of conventional tobacco products such as cigarettes, cigars and smokeless tobacco carefully select the type of tobacco they use in preparing such products, which is predominantly to achieve specific chemosensory effects and nicotine delivery (i.e. sensory appeal and addictiveness). Differences in toxicity is, however, an important by-product of such selection, because the type of tobacco and how it is processed significantly affect the levels of important constituents such as TSNA, PAH, aldehydes and other volatile substances, metals and other toxicants in product contents and emissions *(61,83,84)*. Expanded and reconstituted tobaccos, which are often used in cigarettes, may result in lower nicotine contents but higher emissions of carbon monoxide, aldehydes and PAH *(64,85)*. While cigarette smoke is a complex chemical mixture and its toxicity is the result of the combined effect of several toxicants and carcinogens, prospective epidemiological studies indicate that greater exposure to certain individual smoke carcinogens is associated with a higher risk for cancer, even after adjustment for the amount smoked *(85–87)*. In smokeless tobacco products, higher levels of TSNA are found in products made with tobacco rich in nicotine and other tobacco alkaloids, and higher levels of PAH are found in products made with fire-cured tobaccos *(61)*.

9.3.3.2 Additives, including menthol

Additives used by manufacturers to impart properties that may appeal to users can also be sources of additional amounts of toxicants and carcinogens, in addition to

the inherent toxicity and carcinogenicity of tobacco and its emissions. For example, pyrolysis of sugars added to tobacco filler of cigarettes to improves the taste and smoothness of cigarette smoke and also leads to formation of various toxicants and carcinogens, including furans, aldehydes, PAH and pyridines *(29,88)*. Other chemical ingredients used to improve product taste or aroma, such as limonene, isoamyl alcohol, diacetyl and cinnamaldehyde, are either known toxicants or precursors to known toxicants and carcinogens *(89–91)*.

Some of the effects of additives on the toxicity of ENDS emissions are due to thermal degradation of propylene glycol and flavourants, which leads to formation of various toxicants *(92)*. Other toxic effects may be due to the flavour additives themselves *(93–95)*. One study suggested that menthol may also change the particle size distribution of ENDS emissions, leading to a higher prevalence of smaller particles, which can better deliver nicotine and other constituents deeper into the lungs and the bloodstream of users *(96)*.

9.3.3.3 Product dimensions

Larger tobacco and nicotine product units designed for single use, such as one cigarette or a pouch of smokeless tobacco, are more toxic simply because of the larger amount of tobacco available to burn or to be chewed. The larger amounts of tobacco contain (or are precursors to) larger amounts of toxicants and carcinogens.

The variation in cigarette sizes is well documented, and long, ultra-long and slim cigarettes are available worldwide. It has been shown that the tar and carbon monoxide yields in cigarette smoke increase with increased cigarette circumference *(97)*, and people who smoke longer cigarettes have higher exposure to tobacco-specific constituents, such as nicotine and TSNA, than those who smoke shorter cigarettes *(98)*. Slim cigarettes, however, probably deliver similar levels of formaldehyde, ammonia and phenols as cigarettes of "standard" circumference *(63)*, and a reduction in product dimension may not necessarily reduce toxic exposures unless other product characteristics are standardized.

The plastic packets in which varieties of smokeless tobacco are sold in (such as in India and other South Asian countries) or in pouches (tea bag-like sachets, such as snus in Sweden and the USA) also come in various sizes. Manufacturers sometimes change the single-portion sizes of smokeless products, as observed in the marketing of snus in the USA, or offer the same product in either large or small pouch sizes, which is also true for nicotine pouches.

Dimensions are also relevant to ENDS products. For example, larger e-liquid containers extend the duration in which a device can be used, leading to accumulation of toxic by-products on the internal parts of the device *(99–102)*.

9.3.3.4 Cigarette filters

The overall impact of cigarette filters on health outcomes in people who smoke is not well understood. On the one hand, cigarette filters capture substantial amounts of many toxic and carcinogenic constituents *(64,103)*, in vitro studies have found that the smoke of unfiltered cigarettes is more toxic than that of filtered cigarettes *(104)*, and some studies have reported that smoking unfiltered cigarettes is associated with higher risks for lung cancer than smoking filtered cigarettes *(105–108)*. Other researchers disagree with these conclusions and attributed the reported increases in lung cancer risk to limitations of study design and data analysis as well as potential differences in the tobacco blends used in the two types of cigarette *(109,110)*. Further, while cellulose acetate cigarette filters trap certain chemical constituents in the particulate phase of smoke, they do not substantially affect the components of the gas phase *(111)*. In addition, the minimally biodegradable smoke-coated fibres of cellulose acetate cigarette filters may become detached during smoking and be deposited in the lungs *(112)*. Therefore, filters themselves can pose additional health risks to people who smoke. More details on the potential health impact of cigarette filter are provided in "Cigarette filters: implications for smoking behavior, health effects and the environment" in this report.

9.3.3.5 Filter ventilation

Filter ventilation dilutes cigarette smoke with air and plays a distinct role in the toxicity of cigarette smoke, different from that of the filters themselves. Filter ventilation results in the perceived "lightness" of smoke and results in compensatory smoking to adjust the intake of nicotine (e.g. drawing larger puffs, inhaling more deeply and blocking filter vents) *(113)*. With increasing nicotine intake, such compensatory behaviour lead to similar uptake of toxicants and carcinogens from ventilated as from non-ventilated cigarettes. There is also evidence that filter ventilation increases smoke toxicity by altering the tobacco burning temperature and rate and delivering higher doses of cigarette smoke to deeper compartments of the lung *(114)*. It has been suggested that introduction of filter ventilation may have contributed to the increased incidence of lung adenocarcinoma *(114,115)*, although this may have also resulted from changes in the tobacco primarily used in cigarettes.

9.3.3.6 ENDS device characteristics

Characteristics of ENDS devices that might impact the generation of harmful toxicants in ENDS aerosols include the materials from which various device components are made, the characteristics of the heating coils, the range of power settings associated with the temperature of operation, and whether the e-liquid container is refillable or sealed. The presence of metals in the heating elements

of ENDS leads to release of heavy metal ions to the liquid. There is a substantial body of evidence that metals and metalloids such as arsenic, cadmium, chromium, nickel, copper and lead may be present in ENDS liquids, presenting toxic and carcinogenic risks to users *(116,117)*.

9.3.4 Careful balancing of product design features by manufacturers

As summarized above, manufacturers design tobacco and nicotine products carefully, balancing product characteristics and their combinations. The aim is to maximize and sustain product use by optimizing the appeal of a particular product type and brand to a specific segment of the consumer population, such as youth and women, and enabling product use elasticity (for example, through filter ventilation). In addition, as many product characteristics contribute to chemosensory effects and nicotine delivery, each design feature can be adjusted by manufacturers to compensate for the loss of another due to introduction of a product standard. For example, filter ventilation, which was introduced to achieve lower machine-measured smoke yields, was accompanied by the introduction of longer cigarettes, which contain more tobacco to allow smokers to extract as much nicotine as from shorter, non-ventilated cigarettes *(118)*. As described earlier, use of aromatic tobaccos, which have less sugars and harsher smoke, was balanced by the introduction of added sugars. In response to bans on mentholated cigarettes, the cooling sensation and smoke palatability were replicated by alternative synthetic cooling agents. Toxicity is not the principal consideration of manufacturers when they change the design of tobacco and nicotine products and especially cigarettes. Thus, changes to product design characteristics are often accompanied by increased product toxicity.

9.4 Product standards and how can they be used to reduce use of tobacco and nicotine products

In the context of Articles 9 and 10 of the WHO FCTC *(1)*, a tobacco and nicotine product standard involves setting an upper or lower limit or banning certain product characteristics, including contents, emissions and physical design features. Such standards should include mandating of testing and measurement of such characteristics in tobacco and nicotine products and disclosure of the test results to regulators and the public.

9.4.1 Use of product standards to reduce demand for tobacco and nicotine

In view of the role of product characteristics in the addictiveness and attractiveness of tobacco and nicotine product, establishment of standards can be used to reduce product demand. This, by default, will reduce the population harm inflicted by use of tobacco and nicotine products. In turn, setting limits on certain harmful and

potentially harmful constituents in tobacco and nicotine products may remove the most appealing and addictive products (i.e. those that do not meet the imposed limits) from the market.

9.4.1.1 Product standards to reduce the attractiveness of tobacco and nicotine products

As summarized above, there is a substantial body of evidence that manufacturers use flavours, additives and physical design features to enhance the attractiveness of tobacco and nicotine products. Previous WHO TobReg reports on the scientific basis of tobacco product regulation can be consulted for a more comprehensive, detailed overview of relevant topics. For example, TRS 1001 (cigarette characteristics and design features) *(2)* and TRS 1015 (flavours and sugars in tobacco products, nicotine reduction strategy) *(12)*. The WHO FCTC provides guidance to Parties for regulating such product characteristics *(1)*, and some countries have either implemented or proposed such standards.

Banning flavours. Restrictions on flavours (sometimes specified as characterizing or distinguishable) in some tobacco and nicotine products have been implemented in over 50 countries, including the European Union (EU) member states and Canada, Ethiopia, Nigeria, Republic of Moldova, Senegal, Sri Lanka, Türkiye, Uganda and the United Kingdom, to reduce product attractiveness *(3)*. The policies differ in how flavours are defined, whether menthol and other specific flavours are included and the types of tobacco and nicotine products included. For example, the EU Tobacco Product Directive *(119)* prohibits characterizing flavours (i.e. flavours clearly noticeable during product use and resembling fruit, spice, menthol or other flavours associated with attractive non-tobacco products), while Canada allows certain "traditional alcohol flavours" *(120)*, and Brazil has proposed a ban on all flavouring additives *(121,122)*. The US Family Smoking Prevention and Tobacco Control Act, which was signed into law in June 2009, prohibits any characterizing artificial or natural flavour in cigarettes, including any of its components or parts, except for menthol *(123)*. In 2024, the Food and Drug Administration (FDA) proposed a new product standard that would also ban menthol as a characterizing flavour in cigarettes and all characterizing flavours in cigars *(124)*. The rule was, however, withdrawn in January 2025, before implementation by the new administration *(125)*.

Research on the use of tobacco and nicotine products after flavour restrictions in some countries provides evidence of the beneficial effect of such policies. For example, increased rates of quitting and reduced menthol cigarette use were reported in Canada *(126)*, Netherlands (Kingdom of the) *(127)* and England *(128)*. In the USA, state-wide policies restricting flavours in tobacco and nicotine products have been reported to lead to reductions in the availability of flavoured products and tobacco advertising and to be effective in reducing cigarette and ENDS use *(129–132)*. Concern has been raised, however, about a potential

increase in cigarette smoking in response to flavour restrictions in ENDS *(133)*. The evaluation in Netherlands (Kingdom of the) after the flavour ban showed, however, that 40% of respondents had reduced their e-cigarette use, while 22% reported having quit e-cigarette use altogether; furthermore, most of those who quit because of the ban did not switch to a substitute *(134)*. This indicates that surveillance of market and consumer behaviour should be continued to evaluate any unintended consequences of restrictions.

Restriction of additives. Most regulatory decisions on additives are those that address substances that modify product flavours, with little attention to additives that contribute to the smoothness of products, such as ammonia, sugars, spices and organic acids. The EU Tobacco Products Directive *(119)* bans additives in tobacco and nicotine products that facilitate inhalation or nicotine uptake; however, it does not define such facilitation. Brazil was the first country to propose a general ban on additives (including flavours) *(122)*; however, implementation of this ban has stalled due to tobacco industry lobbying *(135)*.

Restricting addition of ingredients with implied health benefits. The EU prohibits additives and stimulant compounds that are associated in the public mind with energy and vitality, such as caffeine and taurine *(119)*. Other restrictions include ingredients that imply health improvements. This is in line with the recommendation in the Partial guidelines for implementation of Articles 9 and 10 of the WHO FCTC *(1)*. For example, Germany prohibits additives that may give the appearance of a health benefit or reduced health risk (e.g. amino acids) in cigarettes and roll-your-own tobacco *(136)*. Ethiopia and the Republic of Moldova have also introduced bans on such ingredients. Ethiopia's Tobacco Control Directive (No. 28/2015) banned any content or ingredient used to create an impression that a tobacco product has health benefits or reduced health hazards, including vitamins, fruits and vegetables *(137)*. In the same year, the Republic of Moldova passed a law that banned not only caffeine but also vitamins and other, similar additives *(138)*. In Japan, Taiwan (China) and Thailand, tobacco control groups have expressed concern about claims of health for herbal-tobacco products *(42)*; however, no regulatory measures have been implemented.

Banning filters or filter ventilation. While banning filter ventilation is likely to make cigarettes less appealing because of increased harshness, banning filters altogether may be a more effective approach for a more dramatic reduction in the appeal of cigarettes. This is consistent with the recommendation of TobReg in its report to the 157th Executive Board Meeting in May 2025 *(139)*. Although no country to date has restricted cigarette filters or filter ventilation nationwide, Santa Cruz County in California, USA, banned filters in 2024 *(140)*. The EU also has been gaining support for a general ban on cellulose acetate filters *(141,142)*. Further, concern about the misperceptions of the safety of filtered cigarettes, which encourage continued smoking, and environmental concerns about discarding spent

filters, led the Superior Health Council of the Belgian Ministry of Environment to advocate for an EU ban on cellulose acetate filters *(143)*.

Standardizing product dimensions. In Netherlands (Kingdom of the), the dimensions of cigarettes were standardized in 2022 *(144)*. A ban on slim cigarettes (< 7.5 mm in diameter) was also included in the European Commission draft Tobacco Products Directive to eliminate the appeal of such cigarettes to consumers who may consider them less harmful *(54)*; this policy was not, however, included in the final version of the Directive, which instead includes a general statement about monitoring market developments and consumer perceptions of certain products, including slim cigarettes *(119)*. A study of support for a ban on slim cigarettes among smokers in six European countries reported that support was relatively low *(145)*, while misperceptions of the reduced harm of slim cigarettes was particularly high (> 25% of those surveyed) in Hungary, Poland and Romania, where use of slim cigarettes is prevalent. These findings emphasize the importance of public education when considering a ban on slim cigarettes to reduce their appeal to users.

Attractive elements. In Netherlands (Kingdom of the), only cigarettes fabricated with unprinted white paper and a white or imitation cork tip are allowed *(144)*. No other country, however, has banned attractive elements of tobacco and nicotine products, such as the colour of cigarette filter tips or cigarette paper or the style of brand names printed on cigarettes. Such product features are designed to have an aesthetic appeal and are associated with perceptions of reduced harm. Therefore, dissuasive measures such as banning colourful elements, as specified in the Partial guidelines for implementation of Articles 9 and 10 of the WHO FCTC *(1)* and standardizing the print of the brand and the filter tip colour should reduce the attractiveness of cigarettes *(146)*. Another dissuasive approach is printing health warnings on the product itself rather than its packaging. For example, Canada now requires health warnings to be printed on individual cigarettes *(147)*, and similar legislation has been implemented in Australia *(148)*.

9.4.1.2 Product standards to reduce potential dependence on and addictiveness of tobacco and nicotine products

Regulation of the nicotine content of tobacco and nicotine products could be the most effective means of reducing product addictiveness. As other product characteristics that can affect their addictiveness also contribute to product appeal, product standards that address those characteristics can be expected to reduce the potential addictiveness of tobacco and nicotine products *(149)*.

Product standards to reduce the nicotine content of cigarettes. Section 907 of the US Family Smoking Prevention and Tobacco Control Act gives the FDA authority to establish appropriate product standards to protect public health, which may include reduction or elimination of certain harmful constituents in tobacco

and/or cigarette smoke *(123)*. Pursuant to this authority, the FDA has proposed reduction of the nicotine content of cigarettes to non-addictive levels to reduce the dependence potential of cigarettes *(150)*. As recommended in the seventh report of WHO TobReg *(151)*, "Reducing nicotine to ≤ 0.4 mg/g may benefit the broadest population of current and potential smokers." A similar measure was planned in New Zealand *(152)*. The strategy is supported by extensive research showing that switching to cigarettes with very low nicotine content in mainstream smoke, < 0.05 mg, reduces the number of cigarettes smoked per day, decreases dependence on cigarettes and increases smoking quit attempts and cessation *(153–157)*. In addition, young never smokers will be most unlikely to become addicted. Unlike "reduced-yield" cigarettes, in which the nicotine in smoke are reduced by increasing filter and cigarette ventilation, low-nicotine cigarettes are made with tobacco that contains less nicotine than traditional tobaccos; therefore, smoking such cigarettes does not result in compensatory smoking because larger or more frequent puffs do not yield addictive levels of nicotine *(158)*.

While nicotine reduction has not yet been implemented in either New Zealand or the USA, simulation modelling predicts that it will have substantial public health benefits. For example, one model projected that a nicotine reduction standard introduced in USA in 2020 would prevent 8.5 million tobacco-related deaths by 2100 *(159)*. Nicotine reduction alone, however is unlikely to eliminate the addictive potential of cigarettes for all people who smoke and might have to be complemented by other product standards targeting appeal and other intervention and policy measures.

Product standards to limit the nicotine content of ENDS. The EU Tobacco Product Directive *(119)* establishes several regulatory requirements for ENDS, including a maximum nicotine concentration of 20 mg/mL, which has been adopted in many countries outside the EU, including Canada and China, and a maximum volume of 10 mL for refillable e-cigarette tanks and 2 mL for single-use cartridges or pods *(160)*. While the standard was not intended to reduce the addictiveness of ENDS, it does prevent marketing of products with extremely high nicotine concentrations in countries that do not impose such limit and are associated with strong dependence.

9.4.1.3 Product standards to reduce the toxicity of tobacco and nicotine products

The toxicity of tobacco and nicotine products may be reduced by application of some of the product standards described above, either directly (for example, a ban on flavours, sugars and other additives) or indirectly due to reduced appeal and addictiveness, leading to lower intensity and/or amount of product use (for example, reduced-nicotine cigarettes). Another category of product standards that may have a meaningful impact on product toxicity is establishment of limits on toxicants and carcinogens in tobacco and nicotine products, particularly smokeless

tobacco products *(84)*. Examples of proposed standards are listed below, although none has been implemented to date.

Standards for harmful constituents in smokeless tobacco products proposed by WHO. WHO TobReg has recommended that, in smokeless tobacco, the sum of the carcinogenic TSNAs NNN and NNK be limited to 2 μg/g dry weight and that of the carcinogenic PAH benzo[*a*]pyrene be limited to 5 ng/g dry weight *(161)*.

Standards for harmful constituents in cigarette smoke proposed by WHO. WHO TobReg, reiterated in the WHO FCTC Conference of Parties (FCTC/COP/6/14),has also recommended reducing the levels of several harmful constituents in mainstream cigarette smoke, measured under standardized machine-smoking conditions and expressed per mg nicotine, and prohibiting the sale of cigarette brands that have yields above the established limits *(162,163)*. Normalizing constituent levels per mg nicotine was proposed in order to change interpretation of the measurement from the quantity of smoke generated per cigarette, which varies widely among smokers, towards characterization of smoke toxicity generated under standardized conditions.

US FDA proposed standard for N'-nitrosonornicotine in finished smokeless tobacco products. The FDA has proposed a limit on the level of this potent carcinogenic TSNA in finished smokeless tobacco products to be set at 1.0 μg/g of tobacco dry weight *(164)*. This level has been shown to be technically achievable, as certain commercial smokeless tobacco products have done so, such as in snus (made with pasteurized tobacco) sold in Sweden *(61)*. According to FDA estimates, 20 years after implementation of this standard, approximately 12 700 new cases of oral cancer would be prevented and 15 200 life years would be gained in the USA *(164)*. The rates are likely to be much higher in countries with a higher prevalence of smokeless tobacco use.

9.5 Industry tactics

The tobacco industry has consistently resisted any regulatory measure that could interfere with the marketing and sales of tobacco and nicotine products. Their actions include a broad range of tactics, including lobbying, funding selected research, funding organizations and front groups and otherwise seeking to circumvent Article 5.3 of the WHO FCTC and interfering with regulatory and policy decision-making and implementation. Their strategies are not limited to interference with tobacco control measures. In the case of expected or implemented product standards, some manufacturers are engaging in deceptive manipulation of product design to circumvent a standard and/or disguise their non-compliance. The deceptive design of cigarettes marketed in the past as "light" is a well-known example. These cigarettes, which may not be called "light" in Australia, the USA, some other countries or in the EU, include ventilated filters, porous wrapping paper and other elements that reduce smoking machine-measured tar and nicotine

yields. As smokers increase their smoking intensity in response to the reduced nicotine content of the smoke, however, these cigarettes did not reduce smokers' exposure to tobacco carcinogens and therefore did not lower the risk of smoking-induced diseases *(165–167)*. There is evidence that some manufacturers continue to engage in such deceptive practices, not only by manipulating well-established product characteristics but also by leveraging advances in science and technology, examples of which are listed below. Foreseeing such tactics and monitoring products and their marketing is key to maximizing the implementation and public health benefits of a product standard.

9.5.1 Circumvention of flavour bans

In response to imposed and/or expected bans on the use of menthol in tobacco and nicotine products, manufacturers started using the synthetic cooling agents Wilkinson Sword (WS)-3 and WS-23 (also referred to as "koolada") and various "ice"- and "chill"-flavoured products *(168–171)*. Such coolants are used to replace menthol in cigarettes, ENDS liquids and nicotine pouches, and some are marketed as "flavour ban-approved" *(170)*. Another strategy is use of various flavour accessories, such as flavour capsules, drops, sprays, cards, filter tips and tubes or rolling paper for make-your-own cigarettes *(172)*. Deceptive tactics have also been detected in the formulation of "tobacco"-flavoured products after the bans on other flavours, the most frequent being a mixture of fruity and caramel flavours *(173)*.

9.5.2 Circumvention of regulations on nicotine products and/or nicotine standards

Synthetic nicotine-containing ENDS emerged after the US FDA's authority was extended to include all products made of or derived from tobacco *(174)*. Synthetic nicotine is also used in the manufacture of nicotine pouches, which are marketed as "tobacco-free". Such marketing is a familiar strategy to attract consumers interested in "healthier" tobacco and nicotine products. Consequently, the law was changed to extend the regulatory authority of the FDA to tobacco products containing nicotine from any source. Replacement of nicotine with 6-methyl nicotine, a synthetic nicotine analogue, is a bold move by manufacturers to circumvent regulation of nicotine-containing products *(175)*. These products are marketed as containing "metatine" (a trademarked name for 6-methyl nicotine) in various youth-appealing flavours and are advertised as "PMTA exempt", PMTA standing for "premarket tobacco product application" to the FDA, a necessary step for receiving authorization to market a nicotine-containing products in the USA *(176)*.

9.6 Impact and measurement of the effectiveness of product standards

Previous reports by WHO TobReg *(177,178)* noted that tobacco product regulation is a critical pillar of any comprehensive tobacco control programme. Such programmes regulate the contents and emissions of tobacco products by testing and measurement, mandating the disclosure of test results and overseeing the packaging and labelling of such products.

Contracting Parties to the WHO FCTC are obliged to comply with the Convention's provisions on tobacco product regulation, as outlined in Articles 9, 10 and 11. Effective regulation requires government oversight of tobacco product manufacture and enforcement of regulations on their design, contents, emissions, distribution, packaging and labelling, with the goal of protecting and promoting public health. Article 5.2b of the WHO FCTC stipulates that effective regulation should also include, when possible, establishment or reinforcement and financing of national tobacco control and adoption and implementation of effective measures and policies for preventing and reducing tobacco consumption, nicotine addiction and exposure to tobacco smoke.

With other elements of comprehensive tobacco control, assessment of the contents, design features and emissions of tobacco products are expected to contribute to reducing the prevalence of tobacco use and of disease. Both surveillance and research are essential to evaluate the impact of regulations on behaviour and to adapt regulations as necessary.

In its series of handbooks on cancer prevention, the IARC has outlined a framework of measures for assessing the effectiveness of tobacco product regulation *(179)*. While acknowledging that the ultimate test of the impact of a tobacco product standard is a demonstrated reduction in morbidity or mortality associated with the regulation, the handbook addresses practical proximal and distal measures for assessing tobacco product standards, including (i) assessment of the product itself, (ii) monitoring human exposure and biological effects and (iii) conducting surveillance of changes in the design and performance of the product, marketing activity, user perceptions and behaviour and health outcomes. This strategy is similar to the general guidelines for the industry proposed by the US FDA for applications for labelling a tobacco product as "modified risk" *(180)*, for which the FDA requires information on product composition, toxicological risk assessment, human exposure and post-marketing surveillance.

9.7 Implications of findings and research directions

Despite the complexity of product characteristics and their interaction, clusters of product characteristics can be identified that might be considered for inclusion in a comprehensive set of product standards to contribute to reducing the public health

toll of tobacco and nicotine products. The reason is that, as summarized above, manufacturers are consistent in their focus on optimizing product attractiveness and addictiveness to maintain and increase the number of addicted users. Product characteristics and their synergistic impact on the attractiveness, addictiveness and toxicity of tobacco and nicotine products are summarized in Table 9.1.

Table 9.1. Product characteristics and their impact on the attractiveness, addictiveness and toxicity of tobacco and nicotine products

Product characteristic	Attractiveness	Addictiveness	Toxicity	Cumulative impact
Any additives, including flavouring agents, pH modifiers and ingredients that imply a health benefit	↑	↑	↑	Overall harm
Product dimensions, such as cigarette length, circumference and weight; ENDS liquid container capacity; and smokeless tobacco and nicotine pouch size and weight	↑	↑	↑	Overall harm
Any attractive design feature, including bright colours and attractive prints	↑	↑ due to appeal	↑ due to continuous use	Product appeal and (by proxy) overall product harm
Cigarette filters, including any cellulose acetate and ventilated filters	↑	↑ due to appeal and more intense use	↑ due to continuous and more intense use	Overall product harm
Any accessory that may compensate for the removal of additives and filters	↑	↑ due to appeal and elasticity	↑ due to elasticity and continuous use	Product appeal, elasticity and (by proxy) overall product harm
Nicotine in all forms, including tobacco-derived, synthetic and nicotine analogues	↑	↑	↑ due to continuous use	Overall product harm

Research directions to support product standards and measurements of their effectiveness

This review of product characteristics responsible for the addictiveness, attractiveness and toxicity of tobacco and nicotine products and of research on setting product standards to regulate such characteristics indicates the following research gaps and priorities.

- Systematic monitoring should be conducted of the relations among the characteristics of all commercial tobacco products, including heated tobacco products and emerging nicotine products such as electronic cigarettes, and nicotine pouches. Conventional products can be monitored by requiring manufacturers to report product ingredients, contents, emissions and characteristics. Independent academic research with no direct or indirect association with the tobacco or nicotine industry is critical for assessing the characteristics of new

and emerging products. The research should be international to better understand the global range of characteristics.

- Conduct multivariate analysis and modelling to predict changes in product attractiveness, addictiveness and toxicity as a result of the introduction of product standards or combinations of product standards. This could include modelling the impact of nicotine reduction and of banning flavours in cigarettes on product use patterns and the related exposure of people who smoke, as well as the potential impact on uptake of other tobacco or nicotine products.
- Review the range of limits set for nicotine content and emissions for various tobacco and nicotine product categories by countries to determine the optimal limit that will not sustain addiction and determine non-addictive nicotine limits for tobacco and nicotine products for which nicotine limits have not been established.
- Build robust, cost-effective capacity for conducting timely human observational studies, including longitudinal studies of product characteristics, the associated perceptions, use behaviour, exposures and biological effects in users.
- Research should be conducted on communication strategies to prevent consumer misperceptions of product standards as a guarantee of product safety and to counter promotion by the tobacco industry.
- Conduct implementation research on the adoption and implementation of evidence-based interventions for tobacco and nicotine product use cessation.

9.7 Policy recommendations

- Establish standards for product characteristics related to abuse liability (attractiveness and addictiveness), which can have broader impacts on product toxicity and long-term harm. Consider focusing on product characteristics that are relevant to product attractiveness and addictiveness. Specific recommendations for product standards include the following.
  - Ban all additives to all tobacco and nicotine products, including those used in attempts to circumvent additive bans, such as flavours, sugars, novel synthetic substitutes (e.g. synthetic coolants). Member States should consider more inclusive regulations (e.g. banning all compounds that bind to the TRPM-8 receptor).
  - Require reduction of the nicotine content in cigarettes and other smoked products to non-addictive levels.
  - Set a limit on the nicotine content of ENDS liquids.

- Standardize the physical design features of tobacco products to contribute to removal of product elasticity, because a single standard is unlikely to be effective, as industry will adjust other product characteristics to maintain appeal. Comprehensive standards should be based on a comprehensive review of scientific studies related to regulation of the product.
- Devise systems to enforce product standards and require companies to report ingredients, additives, product design features and emissions to national regulatory authorities.
- Anticipate, monitor and counter industry manipulation of product characteristics in response to regulatory measures. The actions should include monitoring and regulating tobacco industry marketing and public relations strategies.
- Mandate disclosure of harmful contents and emissions of tobacco and nicotine products according to the WHO TobLabNet standard operating procedures, when available.
- Support independent academic research to pursue the identified research directions.

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10. Overall recommendations

The WHO TobReg publishes reports to provide a scientific basis for tobacco product regulation. The reports, which are recognized as WHO technical products, are practical, useful resources for use by WHO Member States to support implementation of the WHO FCTC, particularly in relation to Articles 9 and 10, which address the regulation and disclosure of the contents, emissions and design features of tobacco products *(1)*. In line with the requirements of those Articles, with relevant reports and decisions of the COP)to the WHO FCTC and with previous reports of the Study Group, the volumes in the WHO Technical Report Series identify evidence-based approaches to regulating tobacco and nicotine products, including new and emerging products such as ENDS, electronic non-nicotine delivery systems (ENNDS), HTPs and nicotine pouches. The Study Group's reports provide authoritative scientific guidance in the form of recommendations, which are tabled at WHO Executive Board meetings and are available to Parties to the WHO FCTC to consider in fulfilling their obligations *(2)*. Certain recommendations made in the current report were tabled at the 157th WHO Executive Board Meeting in May 2025 *(3)*. The recommendations are relevant in various contexts according to the national regulatory environment, the patterns and prevalence of use of nicotine, tobacco and related products and other factors that have implications for regulation of these products, such as policy goals and capacity for regulation, including bans.

In view of the annual global death toll due to tobacco use and the fact that tobacco is one of the greatest ongoing threats to global health, a key priority is acceleration of tobacco control by reducing its demand. Strong, effective tobacco product regulation plays an essential role in reducing demand for tobacco and nicotine and can thus reduce tobacco use and prevent the burden of tobacco-related diseases. In 2024, about 80% of the world's 1.2 billion tobacco users lived in low- and middle-income countries, where health systems are often less equipped to manage those consequences *(4)*. In an encouraging sign, however, the global prevalence of tobacco use is decreasing, an achievement due largely to persistent, coordinated tobacco control worldwide, including effective product regulation *(5)*. The pace of the decrease, however, remains too slow, and much more must be done to accelerate progress to safeguard public health. TobReg reports complement global work to strengthen implementation of the WHO FCTC, thereby helping to reduce tobacco use and improve overall public health nationally, regionally and globally.

The deliberations, outcomes and recommendations of the twelfth meeting of the Study Group, presented in this report, provide recent updates and developments in tobacco, nicotine and related products that increase their attractiveness, addictiveness and toxicity, such as use of flavours, sugars and specific design features. The rapid development of the tobacco and nicotine market and

the targeted marketing strategies used to expand the consumer base of the tobacco industry not only sustain nicotine dependence among users but also create new pathways for initiation, undermining public health policies and slowing progress in tobacco control policy. This poses challenges for policy-makers and regulators. Therefore, it is critical that TobReg, assisted by subject matter experts, provide robust evidence for regulatory action to maximize the impact of tobacco control measures. TobReg reiterates its recommendation made in a previous report *(6)* to remain firmly focused on evidence-based measures to reduce tobacco use, as outlined in the WHO FCTC, such as smoke-free policies;, comprehensive bans on advertising, promotion and sponsorship; application of graphic health warnings; offering help in quitting and resisting distraction by the tobacco industry and other vested interests; and ensuring that regulations are extended and applied comprehensively to all forms of tobacco and nicotine products, rather than limited to certain products, such as cigarettes.

This report further highlights the importance of:

- reliance on independent, high-quality research as the basis for effective product regulation and policy-making;
- ensuring responsible, transparent reporting of product contents, emissions and design features to strengthen accountability and support evidence-based decisions;
- monitoring and regulation of product and market developments to safeguard public health, with particular attention to protecting children, adolescents and other vulnerable groups from targeted industry practices;
- enforcing strict controls on additives and design features that increase product attractiveness, mask their harshness or encourage youth initiation, thereby reducing the risk of uptake by young people;
- adopting forward-looking regulatory measures to anticipate future product innovations and to ensure that policies remain responsive and effective;
- closing regulatory gaps that could be exploited by the industry, including using harmonized approaches that apply to all tobacco and nicotine products;
- ensuring continued focus on tobacco control to counter nicotine addiction and reduce the prevalence of tobacco use; and
- implementing the recommendations of the Study Group to promote coordinated, evidence-based action among countries and regions.

Chapters 2–9 of the report provide scientific evidence, policy recommendations and guidance to bridge regulatory gaps in tobacco control. The report also

identifies areas for further work and research, including national regulation, while accounting for regional differences, thus providing a strategy for continued, targeted technical support to all countries, especially WHO Member States. The main recommendations of the Study Group are outlined below.

10.1 Main recommendations

The main recommendations to policy-makers and all other interested parties include the following.

- Prohibit the sale of all tobacco, nicotine and related products to children and young people.
- Ban the manufacture and import of all tobacco, nicotine and related products with product characteristics that specifically appeal to children and young people.
- Regulate product characteristics and impose standardized tobacco product design to remove elasticity and variations among products that disproportionally influence their attractiveness, addictiveness or toxicity, such as standardized cigarette length and diameter, and prevent manufacturers from exploiting regulatory loopholes.
- Ban filters to reduce the palatability and appeal of cigarettes, remove consumer misconception about filters substantially reduce health harms, and reduce a major source of toxic tobacco waste, including the microplastics deposited by cellulose acetate in filters.
- Require a reduction in the nicotine content of cigarettes and other smoked products to non-addictive levels.
- Ban all additives to tobacco and nicotine products, including those used in attempts to circumvent bans on additives, such as flavours, sugars and novel synthetic substitutes (e.g. synthetic coolants). Member States should consider more inclusive regulations, such as banning all compounds that bind to the TRPM-8 receptor.
- Recognize the health concerns represented by use of sugars and sweeteners in tobacco and nicotine products, which influence their attractiveness, addictiveness and toxicity, and inform the public about their presence and effects in these products.
- Ignore arguments that addition of sugars represents replenishment of sugars removed during processing of tobacco, and extend the ban to any product manipulation that might enable manufacturers to circumvent a ban on sugars, such as use of novel synthetic substitutes.
- Implement a comprehensive ban on advertising, promotion and sponsorship of all tobacco and related products, as per Article 13 of the WHO FCTC.

- Fully implement the decisions of the WHO FCTC and other tobacco control measures to ban smokeless tobacco products similarly to smoked tobacco products, with particular attention to preventing use of smokeless tobacco among youth.
- Develop standardized classifications and definitions and methods for characterizing all smokeless tobacco products and their constituents to improve tobacco control.
- Mandate disclosure by manufacturers of product characteristics, harmful and potentially harmful contents and emissions of tobacco and nicotine products, including e-cigarettes and smokeless tobacco, and, where applicable, mandate use of the standard operating procedures for the analytical methods recommended by the WHO Tobacco Laboratory Network. The mandate should cover contents and emissions related to aldehydes, heavy metals, sugars and sweeteners, synthetic cooling agents, nicotine analogues and others as appropriate.
- Ensure periodic surveillance and forecasting to better inform regulators about developments in the marketplace. Such systems should include several data streams (e.g. industry disclosures and sales data on product contents and emissions) to provide information on distinctive features of emerging tobacco and nicotine products or product modifications in response to regulations and should focus on trends among children and young adults

Countries are urged to implement the above recommendations, as there is sufficient information on the regulation of tobacco and nicotine products and setting standards for countries to act to protect the health of their populations, especially children, adolescents and young people. Furthermore, to expand global knowledge, market developments and scientific evidence should be monitored, especially for low- and middle-income countries, where surveillance and research capacity are often limited, to bridge any identified gap with research and to learn from country experiences. More evidence, research and country experience are critical to ensure effective regulation, anticipate future product developments and ensure that public health policies remain robust and equitable. Regulators and the public health community should continue to accelerate work to curb tobacco and nicotine use, guided by the evidence-based policies set out in the WHO FCTC) the MPOWER measures *(7)* and relevant decisions of the Conference of the Parties. Countries are encouraged to implement these proven measures, other WHO recommendations and, in addition, to consider the recommendations contained in this report. Specific recommendations on each of the topics addressed are provided in section 2.8; 3.10; 4.12; 5.10; 6.7; 7.9; 8.7; and 9.7.

10.2 Significance for public health policies

The Study Group report provides guidance to Member States in understanding scientific evidence as the basis for regulating tobacco and nicotine products, including cigarettes, smokeless tobacco and new and emerging nicotine and tobacco products. The ninth report of the Study Group addressed nicotine pouches, additives, synthetic nicotine and biomarkers of exposure, as well as social media marketing of tobacco and non-therapeutic nicotine products *(7)*. This tenth report highlights the importance of regulating tobacco and related products to protect children and young people, the new developments and implications of flavours, the update on the science of sugars in tobacco and nicotine products, the potential impact of cigarette filters, the new product developments of cigarettes and its effects, the update on science of aldehydes and metals in e-liquid, the update on the landscape and product regulation of smokeless tobacco, and the product characteristics and relevant standards of tobacco and nicotine products. The report also identifies research gaps and makes recommendations on these matters as part of a broader tobacco control framework. The recommendations address some of the unique regulatory challenges faced by Member States because of the rapid proliferation and development of these products in their markets. In addition, the report updates Member States' knowledge and serves as a ready material to provide guidance for formulating effective strategies in regulating tobacco and nicotine products.

The Study Group, through its unique composition of regulatory, technical, and scientific experts, navigates and distils complex data and research and synthesizes them into policy recommendations to inform policy development at country, regional and global levels. This report, by multidisciplinary experts relevant to the regulation of nicotine, tobacco, and related products, addresses the challenges faced by regulators for effectively regulating these products. Regulators, governments, and other interested parties can rely on the science and evidence provided to formulate regulatory measures to strengthen tobacco control, close regulatory loopholes, and counter industry's arguments, as appropriate. In formulating policies, Member States should focus on the areas most relevant to their policy goals, public health objectives, and regulatory context. The Study Group plays a critical role in guiding this process, by providing technical assistance particularly for governments with limited resources or capacity to address the complex technical issues surrounding tobacco product regulation.

The recommendations of the Study Group promote international coordination of regulatory efforts and the adoption of best practices in regulating tobacco and nicotine products. They strengthen capacity for product regulation across all six WHO regions, provide Member States with a ready scientific resource, and support the implementation of the WHO FCTC by its Parties. Tobacco product regulation complements other provisions of the WHO FCTC aimed at reducing

demand. If effectively implemented, these recommendations would contribute to lowering tobacco use prevalence and improving public health. Given the aggressive promotion of nicotine, tobacco, and related products, globally, the Study Group urges Member States to ensure a continued focus on evidence-based measures to reduce tobacco use as outlined in the WHO FCTC, without entertaining any distractions from tobacco and related industries.

10.3 Implications for WHO programmes

The report fulfils the mandate of the WHO Study Group on Tobacco Product Regulation to provide the Director-General with scientifically sound, evidence-based recommendations for Member States about tobacco product regulation, a highly technical area of tobacco control in which Member States face complex regulatory challenges. The outcomes of the Study Group's deliberations and its main recommendations will improve Member States' understanding of developments in the attractive features of nicotine, tobacco and related products and the promotional strategies used by manufacturers to circumvent regulations and expand their customer base and market.

This report contributes to the body of knowledge on product regulation, which be used by the No Tobacco Unit of the Department of Social Determinants, Promotion and Prevention at WHO in providing technical support to Member States in implementing effective tobacco control policies. It will also update regulators and Member States through the Global Tobacco Regulators Forum and Parties to the WHO FCTC through WHO's report to the Eleventh Session of the Conference of the Parties in November 2025 on technical matters related to Article 9 and 10 of the Convention. The proposed actions will contribute to meeting Sustainable Development Goal target 3.a, to strengthen implementation of the WHO FCTC in all countries *(8)*. It will also contribute to achievement of the global noncommunicable disease targets for 2025, particularly the goal of a 25% relative reduction in the risk of premature mortality from cardiovascular diseases, cancer, diabetes and chronic respiratory diseases and a 30% relative reduction in the prevalence of current tobacco use among people aged ≥ 15 years, and the targets of the WHO Fourteenth General Programme of Work (2025–2028) *(9)*.

This report, a WHO technical product (global public health good), is available to all countries to provide information for reducing tobacco use and improving public health overall.

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WHO study group on tobacco product regulation

This report fulfils the mandate of the WHO Study Group on Tobacco Product Regulation to provide the Director-General with scientifically sound, evidence-based recommendations for Member States about tobacco product regulation. This report presents the outcomes, deliberations and recommendations of the Study Group at its twelfth meeting on eight background papers, which addressed emerging issues in tobacco product regulation, such as protection of the youth, as well as additives that enhances the attractiveness of tobacco and nicotine products, such as flavours and sugars. The eight topics addressed in the report are enumerated below:

1. Regulation of tobacco and related products. Priorities for the protection of children and young people;
2. Flavours in tobacco and nicotine products: new developments, implications and regulation;
3. Science of sugars in tobacco and nicotine products and regulatory recommendations, an update;
4. Cigarette filters: implications for smoking behaviour, health effects and the environment;
5. Evolving design, additives and accessories for cigarettes and effects on addictiveness, attractiveness and toxicity;
6. Aldehydes and metals in e-liquids as potential targets for regulation;
7. Smokeless tobacco: a complex landscape, product regulation and considerations for the future; and
8. Tobacco and nicotine product characteristics and relevant standards.

The report considers the potential impact of the key considerations in the background papers on tobacco control efforts, identifies research gaps and makes some recommendations. The recommendations on each of the topics considered in the report are set out at the end of the relevant section and the overall recommendations of the Study Group are summarized in the final section of the report. These recommendations directly address some of the unique regulatory challenges faced by Member States due to direct and indirect advertising, as well as product and market developments. In addition, the report will update Member States' knowledge and aid the formulation of effective regulatory strategies for nicotine and tobacco products.

The report, which is a WHO technical product (i.e. an initiative developed or undertaken by WHO that is of benefit either globally or to many countries in many regions), is available to all countries to help drive impact at country level and globally, towards reducing tobacco use and improving overall public health.