

Contents

1. Introduction	1
1.1 Background	2
References	5
2. Contents and design features of tobacco products: their relationship to dependence potential and consumer appeal	7
2.1 Background	7
2.2 Terminology	8
2.3 Relationship between dependence potential and harm	10
2.4 Effect of contents and designs on dependence potential	11
2.4.1 Nicotine dose level	11
2.4.2 Other contents	11
2.4.3 Modifying nicotine delivery speed and efficiency by pH and free nicotine control	11
2.5 Regulatory implications and challenges	13
2.5.1 Personal and local vendor-made products	15
2.5.2 Nicotine levels	15
2.5.3 Assessing and regulating dependence potential	15
2.6 Conclusions	16
2.7 Research needs	17
2.8 Regulatory recommendations	18
References	20
3. Candy-flavoured tobacco products: research needs and regulatory recommendations	25
3.1 Introduction	25
3.2 Purpose of the recommendations	25
3.3 Background	26
3.4 Description of flavoured tobacco products	28
3.4.1 Flavoured brands	28
3.4.2 Flavour application	34
3.5 Regional and global patterns of flavoured tobacco product use	35
3.6 Impact on public health	37
3.7 Science base and conclusions	38
3.8 Research needs	38
3.9 Regulatory recommendations	39
References	40
4. Biomarkers of tobacco exposure and of tobacco smoke-induced health effects	43
4.1 Introduction	43
4.2 Background	43
4.3 Biomarkers: definition and description	45
4.4 Measuring exposure	45
4.5 Measuring injury and disease	47
4.6 Existing evidence on biomarkers	47

4.7	Specific biomarkers	48
4.7.1	Tobacco alkaloids	49
4.7.2	Minor tobacco alkaloids	51
4.7.3	Other particulate phase components	52
4.7.4	Gas phase components	53
4.7.5	DNA and protein adducts	54
4.7.6	Mutagenic activity of the urine	56
4.8	Measuring biological changes	56
4.8.1	Assessing oxidative stress	58
4.8.2	Measures of inflammation	58
4.8.3	Measures of endothelial dysfunction	59
4.8.4	Measures of clotting	59
4.8.5	Insulin resistance	60
4.8.6	Circulating endothelial precursor cells	60
4.8.7	Femoral and internal carotid artery intima-media thickness	60
4.8.8	Sister chromatid exchanges in peripheral lymphocytes	60
4.9	Summary of existing biomarkers	60
4.10	Recommended uses for biomarkers of exposure and effect	64
4.10.1	Improving the accuracy of the definition of current tobacco use status	64
4.10.2	Evaluating the intensity of exposure to specific constituents	66
4.10.3	Evaluating the intensity of exposure as a proxy for total tobacco exposure	68
4.10.4	Measuring reduced injury or harm	69
4.11	Summary of biomarker recommendations	70
	References	72
5.	Setting maximum limits for toxic constituents in cigarette smoke	77
5.1	Introduction	77
5.2	Regulatory strategy	80
5.3	Selection of the machine-testing method	83
5.4	Criteria for selecting constituents for regulating maximum limits	85
5.5	Specific regulatory recommendations for TSNAs	89
5.6	Interpretation of the maximum limit values	92
5.7	Communication of the results of the testing to the public	92
5.8	Methods for measuring nitrosamines	93
5.9	Considerations for modified cigarettes and potential reduced exposure products	94
5.10	Future directions	95
	References	96
6.	Overall recommendations	99
6.1	Contents and design features of tobacco products: their relationship to dependence potential and consumer appeal	99
6.2	Candy-flavoured tobacco products: research needs and regulatory recommendations	100

6.3	Biomarkers of tobacco exposure and of tobacco smoke-induced health effects	101
6.4	Setting maximum limits for toxic constituents in cigarette smoke	102
	Acknowledgements	105
	Annex 1	107
	Reports and other documents arising from meetings of the WHO Scientific Advisory Committee on Tobacco Product Regulation (SACTob)	107
	Statement of principles guiding the evaluation of new or modified tobacco products (2003)	107
	Recommendation on nicotine and its regulation in tobacco and non-tobacco products (2002)	107
	Recommendation on tobacco product ingredients and emissions (2003)	108
	SACTob recommendations on health claims derived from ISO/FTC method to measure cigarette yield (2003)	108
	Recommendation on smokeless tobacco products (2003)	109
	Annex 2	111
	Reports and other documents arising from meetings of the WHO Study Group on Tobacco Product Regulation (TobReg)	111
	Guiding principles for the development of tobacco product research and testing capacity and proposed protocols for the initiation of tobacco product testing: recommendation 1 (2004)	111
	Best practices in tobacco control: regulation of tobacco products: Canada report (2005)	111
	Advisory note: waterpipe tobacco smoking: health effects, research needs and recommended actions by regulators (2005)	112