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Further development of the partial guidelines for implementation of Articles 9 and 10 of the WHO FCTC

Report by WHO

INTRODUCTION

1. This document was prepared in response to the request made by the Conference of the Parties (COP) at its sixth session (Moscow, Russian Federation, 13–18 October 2014), which invited WHO to:

i. Finalize, within one year, the validation of the analytical chemical methods for testing and measuring cigarette contents and emissions in accordance with the progress report presented by WHO to COP at its fifth session (document FCTC/COP/5/INF.DOC./1);

ii. Assess, within two years, whether the standard operating procedures for nicotine, tobacco-specific N-nitrosamines (TSNAs) and Benzo[a]pyrene (B[a]P) in cigarette contents and emissions are applicable or adaptable, as appropriate, to tobacco products other than cigarettes, including smokeless tobacco and waterpipe smoke;

iii. Prepare a report based on scientific evidence on specific cigarette characteristics of interest, including slim/super slim designs, filter ventilation, and innovative filter design features including flavour-delivering mechanisms such as capsules, to the extent that those characteristics affect the public health objectives of the WHO FCTC, for consideration by the working group at its first meeting following the sixth session of the COP;

iv. Continue to monitor and follow closely the evolution of new tobacco products;

v. Prepare a report on the toxic contents and emissions of waterpipe and smokeless tobacco products; and

vi. Report back to the COP through the Convention Secretariat.

2. This report incorporates the deliberations and scientific recommendations from the eighth meeting of the WHO Study Group on Tobacco Product Regulation (TobReg)[1] held in Rio de Janeiro, Brazil on 9–11 December 2015. All annexes to this report can be found on the WHO website[i].

I. Update on the validation of the standard operating procedures for cigarette contents and emissions can be found in FCTC/COP/7/INF.DOC/1.

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[i] http://who.int/tobacco/industry/product_regulation/further-development-articles-9-10-fctc-cop7/en/index.html

II. Applicability of the standard operating procedures for nicotine, tobacco-specific N-nitrosamines (TSNAs) and B[a]P in cigarette contents and emissions to tobacco products other than cigarettes, including smokeless tobacco and waterpipe smoke[ii]:

A. Smokeless tobacco products (SLT)[iii]:

3. ***Nicotine:*** The determination of nicotine in SLT is based on WHO TobLabNet Official Method SOP 04: Standard Operating Procedure for Determination of Total Nicotine in Cigarette Tobacco Filler (WHO TobLabNet SOP 04)[2]. The nicotine ranges in SLT are comparable or slightly higher, by gram, to those reported in cigarette tobacco filler.

4. The determination of total nicotine should be augmented to include measurements of pH and moisture content. Total nicotine measures the entire amount of nicotine in a product regardless of its ionic form. The un-ionized form of nicotine is more readily absorbed in the body. With the total levels of nicotine and pH, the levels of un-ionized nicotine can be determined. Moisture of the product should also be measured so that nicotine (and other contents) can be reported both on a dry and wet weight basis, as variation in moisture affects the concentration of nicotine.

5. Moisture and pH analyses are not part of WHO TobLabNet SOP 04. These additional measurements are not complex and only require equipment such as a drying oven capable of maintaining a temperature of 99 to 1000°C for several hours and a balance to determine weight differences after drying. One method, a modification of AOAC Method 966.02[iv], determines water and tobacco constituents that are volatile at temperatures of 99 ± 1.0°C[3]. Likewise, the SLT pH can be determined using a standard pH meter.

6. ***TSNAs***: The sample preparation and analytical methodology of WHO TobLabNet Official Method SOP 03: Standard Operating Procedure for Determination of Tobacco-Specific Nitrosamines in Mainstream Cigarette Smoke under ISO and Intense Smoking Conditions (WHO TobLabNet SOP 03) can be adapted for the measurement of NNN and NNK in SLT. Adaptations to SOP 03 are based on a comparison with the current CDC method for TSNAs in mainstream smoke emissions and tobacco content[4]. Differences include that (a) the upper calibration curve needs to be extended as some SLT have higher NNN and NNK concentrations (and also kept linear); (b) the SLT samples need grinding and filtering in order not to clog the injection system.

7. ***B[a]P:*** The WHO TobLabNet Official Method SOP 05: Standard Operating Procedure for Determination of Benzo[a]pyrene in Mainstream Cigarette Smoke under ISO and Intense Smoking Conditions (WHO TobLabNet SOP 05) is applicable for the determination of determination of B[a]P in SLTs[5].

8. ***Recommendations***: The WHO TobLabNet methods for TSNAs, B[a]P and nicotine can be adapted or applied to a number of SLT. Further product-specific analysis is needed to cover the entire range of SLT, especially products prevalent in South Asia that have currently not been selected by the TobLabNet due to lack of relevant laboratory expertise and/or capacity. SLT also contain metals,

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[ii] For the list of laboratories who have participated in the validations, please refer to Annex 1.

[iii] A total of seven SLT products (1 snus, 4 moist snuff, 1 dry snuff, and 1 loose leaf) were selected by the United States Centers for Disease Control and Prevention (CDC) for this study. Four of the products were reference products obtained from CORESTA (snus, moist snuff, dry snuff, loose leaf) and three commercial moist snuff products were obtained from a commercial vendor. CDC shipped these seven SLT products to China National Tobacco Quality Supervision & Test Center (CNTQSTC), China and Health Sciences Authority (HSA), Singapore for the method verification.

[iv] AOAC 966.02 Loss on Drying (Moisture) in Tobacco, Gravimetric Method.

humectants, aldehydes and many other toxicants[v], and further work is needed to recommend standard quantitative analysis procedures.

9. Parties are invited to consider requiring SLT manufacturers to disclose pH level and toxicants (TSNAs, B[a]P and nicotine) using WHO recommended methods/SOPs, as currently recommended for cigarettes, from approved laboratories.

B. Waterpipe tobacco

10. Of the three validated TobLabNet SOPs for the determination of cigarette contents, the humectants and nicotine methods were investigated for adaptation to waterpipe tobacco based on expert recommendations. In order to determine the TSNA content of waterpipe tobacco, it is necessary to develop and validate a new analytical method.

11. ***Nicotine:*** Nicotine determination in cigarette tobacco filler is described and validated in WHO TobLabNet SOP 04. Waterpipe tobacco contains high levels of humectants and various types and amounts of flavours which might interfere with nicotine analysis. Changing chromatographic parameters to avoid co-elution of interfering flavours is time-consuming and complex due to the high amount of different flavourings used in waterpipe tobacco. A more practical approach for measuring nicotine content in waterpipe tobacco is to use gas chromatography-mass spectrometry (GC-MS).

12. ***Humectants:*** WHO TobLabNet SOP 06 for the determination of humectants in cigarette tobacco filler is validated for glycerol, propylene glycol and triethylene glycol. Due to the much higher levels of glycerol in waterpipe tobacco, special precautions have to be made in the GC-MS and GC-FID analyses to avoid co-elution of glycerol and triethylene glycol. Also, the calibration range of glycerol and propylene glycol needs to be adjusted due to the higher levels of these chemicals in waterpipe tobacco.

13. TobReg found that toxicant emissions are dependent on a combination of variables such as the waterpipe device itself, the charcoal, the tobacco product and puff topography. The Beirut Method can be used to generate waterpipe smoke for the purpose of analysis since waterpipe puff topography is characterized by much larger puff volume, flow rate, and puff number compared to cigarette smoking[6]. Further research is necessary to determine whether existing WHO TobLabNet methods to determine cigarette emissions can be used to test waterpipe emissions. Certain aspects of the waterpipe, such as the addition of flavourings, could interfere with the results measured by current methods.

14. ***Recommendations***: Parties are invited to consider an approach which focuses on measuring and reporting the chemical contents known to contribute to the toxicity, addictiveness and appeal of waterpipe tobacco smoking, rather than regulating the emissions of the waterpipe tobacco product. Parties should also consider specifying that WHO TobLabNet SOPs 04 and 06 (for nicotine and humectants) be used by laboratories performing the tests.

15. Parties can initially require the reporting of harmful contaminants that have been found in products marketed for waterpipe use, as explained in Annex 2 of this report. As evidence and standardized measurement methods become available, Parties could eventually require the reporting of chemicals which are found to contribute to the toxicant emissions listed in Annex 3 of this report.

III. Specific cigarette characteristics of interest

[v] Please see paragraph 38.

A. **Physical dimensions: diameter, length and packing density**

16. The usual diameter of a conventional cigarette is 7.5 to 8 mm, while slim varieties have diameters of 5 or 6 mm[7]. Length and circumference of cigarettes influence their appeal and harm perceptions. Longer and slimmer cigarettes are widely acknowledged to increase perceptions of stylishness and to generally appeal to women[8,9], and have been associated with weight control[10]. Slim and super-slim cigarettes also led to perceptions of lower harm among 15-year-old study participants[11].

17. The amount of tobacco consumed varies with the circumference of the cigarette. As circumference increases, tar and CO yields increase[12]. In cigarettes with smaller circumference, emissions to the smoker decrease accordingly[13]. Decreasing the cigarette circumference while keeping the packing density constant reduces the amount of tobacco available for burning and allows a greater volume of oxygen utilization during combustion. This reportedly results in a reduction in yields of some smoke emissions including tar, nicotine, CO, and several volatile smoke constituents[14].

18. On the other hand, decreasing cigarette circumference increases flow rates, which reduces the amount of time for the smoke to pass to the mouth (residence time) and decreases the filtration achieved by the tobacco rod and retention by the filter. Factors that reduce filtration by the tobacco rod or retention by the filter may result in higher levels of smoke emissions[15]. The puff-by-puff delivery of emissions is inversely related to cigarette length because longer cigarettes have a smaller circumference which provides less tobacco for combustion per puff and because dilution of oxygen through the wrapper is likely to be primarily responsible for changes in smoke concentrations[16].

19. The mediating effect of cigarette length on smoke composition also depends on the packing density of tobacco. Two factors influence smoke emission with respect to packing density. As packing density increases, there is more tobacco mass to burn during puffs and there is a corresponding increase in chemical emissions in mainstream smoke. However, smoke constituents are filtered as smoke is drawn through the tobacco rod. In one study of cigarettes of different packing densities that were machine-smoked to predetermined lengths, nicotine and smoke condensate yields were lower in cigarettes with higher packing density and greater in cigarettes with lower packing density[17].

B. Filter ventilation

20. Filter ventilation is achieved through the combined use of porous plug wrap and perforated or porous tipping paper. The degree of ventilation or dilution achieved depends on the porosity of the plug wrap, the extent of tipping-paper perforation or porosity, and the location of the perforations[18].

21. Filter ventilation changes users' sensory responses to cigarette smoke and affects consumer perceptions of the relative harm associated with low-yield cigarettes. Specifically, filter ventilation in low-yield cigarettes leads to perceptions of smoke tasting lighter and being less irritating than regular cigarettes, supporting the belief that tar and nicotine intakes are reduced[19,20,21].

22. Filter ventilation and subsequent smoke dilution with air result in compensatory smoking behaviours, such as drawing larger puffs, inhaling more deeply, and blocking filter vents to prevent smoke dilution. Most smokers seek to optimize their nicotine intake, which is associated with the perceived chemosensory impact, to achieve rewarding sensations and to avoid the aversive sensations associated with nicotine withdrawal[22,23]. Filter ventilation is often counteracted by vent blocking by smokers' fingers or lips, with many smokers of light and ultra-light cigarettes often unaware that they are doing it[24,25]. Such compensation is likely to be complete for most smokers who switch from higher yield to lower yield cigarettes[26].

C. Flavours

23. Overall, research shows higher use of aromatized cigarettes by women and young people, those aware of smoking-related health risks, and those who perceive some cigarettes to be less harmful than

others[27,28]. Various flavours including menthol, spearmint, peppermint, chocolate, apricot, coconut and marshmallow were used to address aftertaste concerns and aroma preferences among women[29]. Flavoured tobacco products generally appeal to young adults and adolescents and are often marketed to them[30,31,32].

24. Besides their potential marketing appeal to youth and non-smokers, there is concern that flavours in cigarettes might mask smoke harshness, making inhalation easier. Sensory qualities of menthol, the most commonly used flavouring additive, may contribute to perceived smoothness, and increase the appeal associated with smoking. Smokers of mentholated cigarettes smoke their first cigarette of the day sooner than smokers of non-mentholated cigarettes, pointing toward a greater motivation to smoke mentholated cigarettes[33]. In addition, smokers of mentholated cigarettes attempt to quit more often but succeed less often, which suggests that mentholated cigarettes may be more addictive than non-mentholated ones[34,35].

25. ***Recommendations (for A, B and C above):*** As stated in the Partial Guidelines for Articles 9 and 10, Parties should require that manufacturers and importers of tobacco products disclose the information on design features listed in Appendix 2 of the Partial Guidelines to governmental authorities at specified intervals, including the results of tests conducted by the tobacco industry. Parties should also consider restricting or prohibiting other design features that may increase the attractiveness of tobacco products, such as flavours and capsules. In order to establish and maintain the consistency of data reported to them by the tobacco industry, Parties should also recommend methods for reporting these design features.

26. Parties should ensure that every manufacturer and importer provide governmental authorities with a laboratory report showing a test was performed for the measurement of a particular design feature, as well as the proof of accreditation of the laboratory which performed the analysis. Lastly, should there be any change to the design features of a particular brand of tobacco product, Parties should require that manufacturers notify governmental authorities of the change and provide updated information when it is applied.

IV. Evolution of new tobacco products

27. An increasing number of new tobacco products, especially alternatives to cigarettes, are or will be marketed with the claim that they can reduce exposure to harmful chemicals in tobacco smoke. Some of the more recent products heat rather than burn tobacco. The industry has claimed that the quantity of toxicants generated by these devices is significantly lower compared to standard cigarettes.

28. One such device is Ploom, which electronically heats tobacco, generating a vapour which users inhale. Marketing emphasizes its lack of combustion and smoke, which allows tobacco intake in the presence of non-smokers[36]. The Ploom device is loaded through a removable mouthpiece with a small capsule filled with moistened, finely shredded tobacco or herbal mix, and powered by a rechargeable battery. The tobacco is placed in prefilled cups intended for single use (pods). The tobacco appears to have been ground to a powder, moistened to make a kind of slurry, and then dried. The cups are covered by aluminium foil, which is punctured by the mouthpiece when connected to the housing. Users activate Ploom by pressing a button. The device maintains a temperature of 160°F.

29. Other novel products include iFuse and iQOS. The iFuse heats a liquid containing nicotine into an inhalable vapour, which then passes through a tobacco section. The iQOS is a pen-shaped device which heats sticks containing tobacco and a filter. The tobacco looks like reconstituted tobacco processed to form a roll of sheet tobacco. The filter part consists of a roll of curled plastic with a filter piece similar to a regular cigarette filter. A metal plate, powered by a rechargeable battery, heats the tobacco inside the stick. Like the Ploom, the device remains active and warm until the button is pressed again and the light turns off. Other available products can be used with a conventional cigarette where the cigarette is also heated and not burned.

30. As previously discussed, products that heat rather than burn are claimed to be less harmful than traditional cigarettes, although these claims of risk reduction are based on industry-funded studies. Independent studies should be conducted to investigate these claims. Convincing evidence has yet to be provided for the claims of risk reduction and health benefits of products that heat rather than burn tobacco[37]. Some scientists consider these heated tobacco products to be just as harmful as conventional cigarettes[38].

31. It would be prudent for Parties to take note of nicotine inhaler technology. The tobacco industry is developing or buying this technology, which would not require heating the nicotine solution[39,40,41]. Further research is needed on the associated health risks.

32. Parties should also be cognizant of vaporizers, which are primarily advertised for use as aromatizers for herbs. However, some of these devices can be used for heating tobacco. The devices are sold separately from the contents, which makes it more complicated to regulate them as tobacco products. Most of these products are powered by rechargeable batteries; however, there are also products that use an internal lighter powered by a refillable butane gas tank to heat the vaporizer. Vaporizers have been developed further to include cellular functions[42].

33. The methods used for testing conventional cigarettes might have to be adapted, or new methods developed, because the puffing behaviour, physical and chemical characteristics (particularly of inhaled aerosols) and user exposure to these new products would differ.

34. ***Recommendations:*** All new and emerging tobacco products should be regulated under the WHO FCTC. This should include products such as vaporizers and any other novel devices which can be used for tobacco consumption and are not classified as electronic cigarettes. When regulation under the WHO FCTC is not feasible, novel products should be monitored to determine their health effects.

V. Toxic contents of SLT and toxic contents and emissions of waterpipe tobacco products

A. SLT

35. SLT have been classified as Group I (known human carcinogens) by the International Agency for Research on Cancer (IARC)[43]. Given the heterogeneity of SLT, it is difficult to identify a standard set of toxicants. Analysis of various SLT shows that there are more than 40 compounds/agents that have been identified as carcinogens by IARC[44,45], which have been found in SLT in various concentrations.[46] Many of the toxic chemicals present in SLT are organic, inorganic and microbiologic components and their by-products during the processing and/or manufacture of SLT[47,48,49,50]. Alkaline agents added to manufactured SLT include carbonates, bicarbonates and slaked lime (calcium hydroxide)[51,52,53,54].

36. SLT are often augmented with additives to mask their harsh tastes, enhance their appeal and facilitate product use[55],[56]. Additives could include chemical flavourants and humectants. Humectants (typically propylene glycol and glycerol) are added to maintain moisture. Table 4 (Annex 4) lists the carcinogens, toxicants or biologically active compounds in SLT.

37. ***Recommendations***: SLT manufacturers could reduce levels of toxicants such as TSNAs and/or to use technologies that reduce exposure to SLT carcinogens. However, manufacturers have generally failed to do so, partly due to Parties' lack of comprehensive regulatory policies on SLT. Specifically, Parties have the opportunity to monitor and regulate pH and nicotine, metals, PAH, TSNA, and nitrite content among other toxicants. The technology required to test pH, nitrate/nitrite and microbial contamination is not expensive and could be implemented in most countries. While framing the SLT regulatory policy, Parties need to carefully review the range of SLT available and keep in mind the heterogeneity of SLT products.

38. When applying the Partial Guidelines for Articles 9 and 10, Parties are invited to consider banning or restricting the use of flavourings and additives which increase the attraction of SLT products and facilitate product use. Furthermore, Parties should also consider a requirement that manufacturers improve storage conditions such as refrigerating products before sale, affixing the date of manufacture on SLTs, as well as regulating packaging materials and requiring manufacturers to educate retailers on the effect of SLT storage conditions.

B. Waterpipe tobacco

39. Waterpipe smoke includes constituents that are transferred from the raw material (e.g. heavy metals, nicotine, tobacco specific nitrosamines), constituents which are chemically synthesized during smoking (e.g. CO, nitric oxide), and constituents which are both transferred and synthesized *in situ* (e.g. polyaromatic hydrocarbons, PAH)[57]. Because waterpipe smoking normally utilizes burning charcoal as the heat source, waterpipe smoke includes toxicants emitted from the charcoal in addition to those from the tobacco product itself. Thus the composition of both the charcoal and the tobacco preparation can influence smoke constituents. A large fraction of the PAH and heavy metal content of waterpipe smoke may be accounted for by the PAH content of raw charcoal, and the metal content of Maasal products (flavoured waterpipe tobacco), respectively[58]. These constituents were found to vary across products, suggesting that regulatory actions limiting toxicant content may be feasible.

40. Because published reports on waterpipe toxicant yields are specific to particular combinations of charcoal and tobacco product, puffing protocol, and waterpipe design, the reported toxicant content varies widely. Nonetheless, all studies to date[59] point to the same conclusion: during a typical waterpipe session, the user will draw large doses of toxicants ranging from less than one to dozens of cigarette equivalents, depending on the toxicant in question. These toxicants are linked to addiction, heart and lung diseases, and cancer.

41. Importantly, reports of toxicant emissions in waterpipe smoke have been corroborated by biomarker assays in smokers, which have shown that users are systemically exposed to CO, nicotine, polyaromatic hydrocarbons, and tobacco specific nitrosamines[60,61,62,63,64,65]. In addition, differences in systemic toxicant exposure patterns between cigarette and waterpipe smokers mimic the differences found in measured toxicant emissions from these smoking methods (e.g. on a nicotine-normalized basis, greater CO exposure, greater PAH exposure, and lower TSNA exposure for waterpipe smokers compared to cigarette smokers). Such agreement provides confidence in the findings to date that waterpipe smoke contains and delivers large doses of toxicants. Table 3 (Annex 4) lists the carcinogens, toxicants or biologically active compounds in waterpipe tobacco products.

42. ***Recommendations:*** Policy options and suggested actions for Parties are explained in detail in paragraphs 15-26 of FCTC/COP/7/10.

ACTION BY THE CONFERENCE OF THE PARTIES

43. The COP is invited to note this report and provide further guidance.

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[1] World Health Organization. WHO Study Group on Tobacco Product Regulation (TobReg). http://www.who.int/tobacco/industry/product_regulation/tobreg/en/

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