Regulating Smokeless Tobacco Products

KH-Smokeless Tobacco
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Smokeless Tobacco

Challenges for Regulation

- Heterogeneity of tobacco products
- Contents and emissions
- Agricultural practices
- Manufacturing practices
- Cultural practices

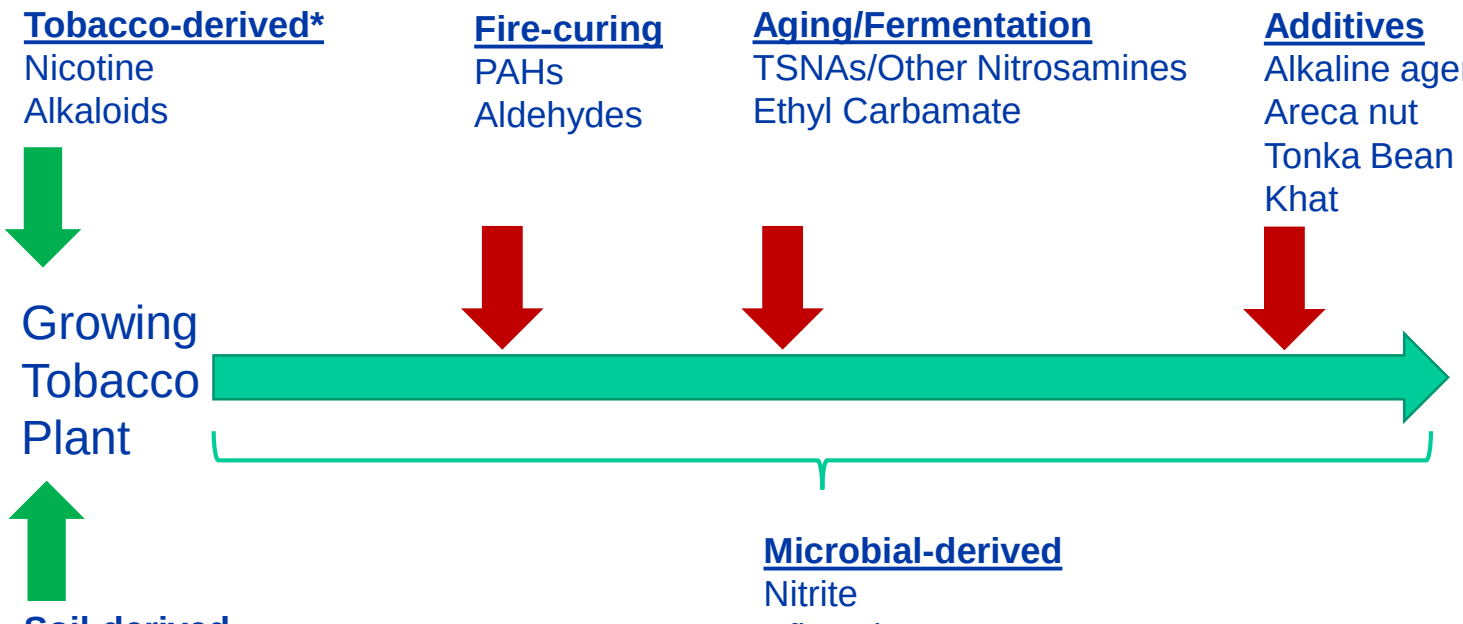
Targets for Product Regulation

- Toxicants in ingredients (tobacco leaves, flavorings and additives, heavy metals, etc)
- Toxicants in emissions
- Addictiveness (Dependence Potential)
- Attractiveness
- Design features

Tobacco Contents & Emissions

- At least 4000 chemicals have been identified in SLT products
- Many proven to be toxicants and carcinogenic

Accumulation of Toxic Chemicals: Farm to Package



Smokeless tobacco can contain live microbes at the time of use

* Organic constituents of tobacco are impacted by tobacco species and type, growing conditions, climate, soil, etc.

- In regulating tobacco products, the larger the number of toxicants regulated, the more distortion will be in the existing market and the more complex will be the regulatory oversight process.

- TobReg effort focused on identifying a reduced number of compounds that would balance the concerns identified with the practical reality of a regulatory structure.

Toxicity Indices

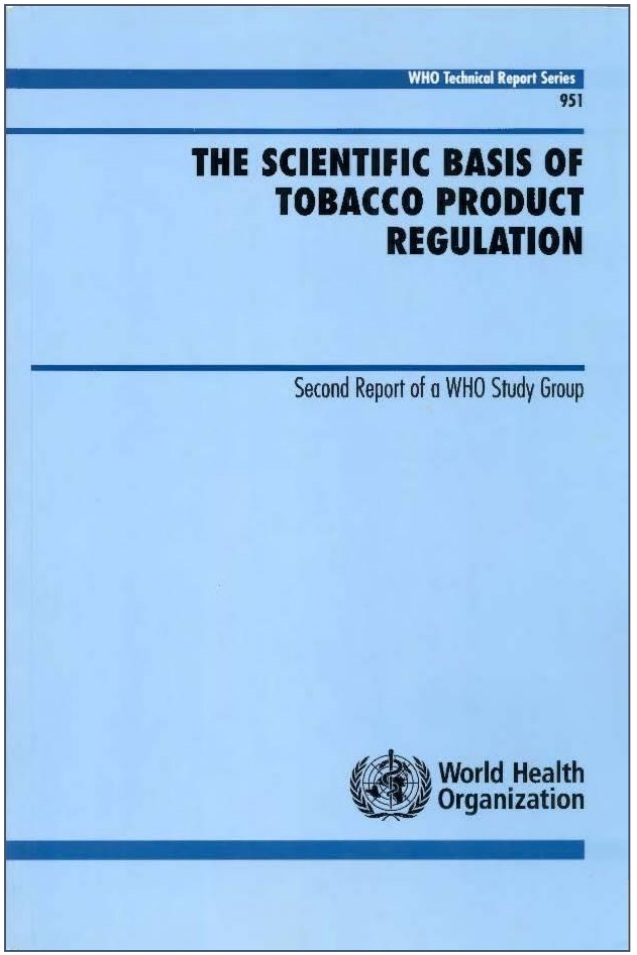
- **Fowls and Dybing** (Tobacco Control 2003;12: 424-430)

1. A simplified system for characterizing hazards of components in cigarette smoke by calculating cancer risk and non-cancer risk indices.

2. This system involves multiplying the yields of individual toxicants with cancer and non-cancer potency factors.

Publications of the WHO Study Group on Tobacco Product Regulation (TobReg)

WHO Study Group on Tobacco Product Regulation **(TobReg)** Technical Report Series **(945, 951, 955, 967, & 989)**



Chemicals &Toxicants in SLT

- Nicotine
- TSNA (e.g. NNN,NNK)
- Polycyclic aromatic hydrocarbons
  (e.g. benzo(a)pyrene)
- Heavy metals (e.g. Pb, Cd, Cr, As, Ni)
- Nitrates & nitrites

Concentrations of metals and yields of extractable metals reported in smokeless tobacco (µg/g tobacco)

	Ghana	Canada	India	USA (Study 1)	USA (Study 2)
Al	3006 - 5167	NR	NR	NR	NR
As	0.108 - 0.256	0.143 - 0.437	0.1 - 3.5	NR	0.13 - 0.29
Ba	110 - 203	NR	NR	NR	38 - 158
Be	NR	NR	NR	NR	0.010 - 0.038
Cd	1.06 - 1.11	0.30 - 1.09	0.1 - 3.1	0.73 - 1.58	0.66 - 1.88
Co	0.056 - 0.201	NR	NR	NR	0.26 - 1.22
Cr	0.95-1.41	0.71 - 2.19	5.25 - 21.9	NR	0.86 - 3.20
Cu	18.5 - 27.7	NR	9.02 - 61.5	NR	NR
Fe	2433 - 6982	NR	354 - 3213	NR	NR
Hg	0.007 - 0.012	NR	0.02 - 0.11	NR	NR
Mn	121 - 139				
Ni	NR	0.84 - 2.05	1.33 - 13.1	NR	1.39 - 2.73
Pb	NR	0.23 - 1.20	1.76 - 13	0.27 - 2.96	0.28 - 0.85

Measures to Reduce Toxicants

- Reduce the use of *Nicotiana rustica*
- Sun or flue curing of tobacco during manufacturing rather than fire curing
- Pasteurization as compared to fermentation
- Avoiding storage for prolonged periods in warm weather

Mean of Total Nicotine

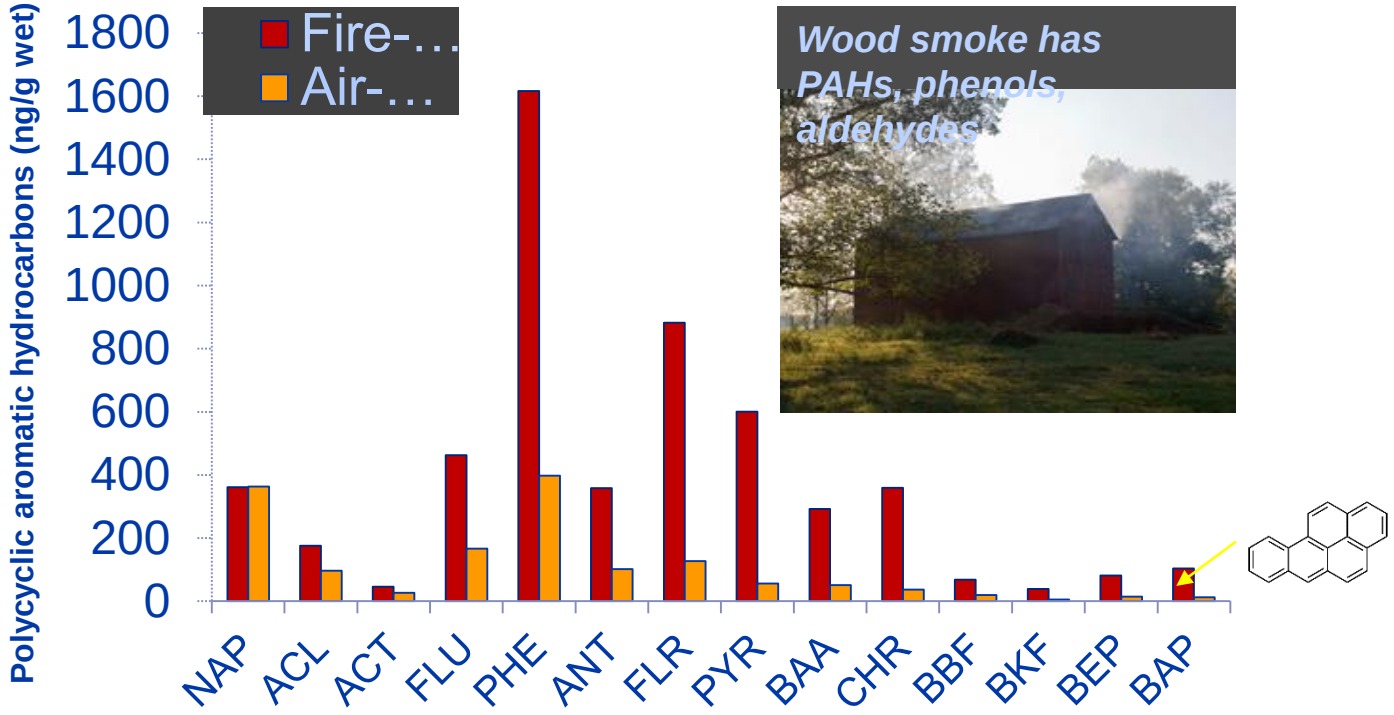
Country	Products	Total Nicotine mg/g
Bangladesh (5 brands)	Gul Powder, Sada Pata, Zarda	23.61 [9.55-34.1]
India (15 brands)	Raja, Gutkha	3.92 [0.91-30.4]
Pakistan (7 brands)	Gutkha, Mawa, Mainpuri, Naswar,	4.26 [0.16-14.2]
Sudan (4 brands)	Toombak	14.69 [9.36-28.2]
Nigeria (2 brands)	Snuff	4.95 [2.49-7.41]
South Africa (9 brands)	Snuff, Snus	11.02 [1.17-17.2]
Sweden (5 brands)	Snus	9.44 [7.76-15.2]
Uzbekistan (1 brand)	Nasway	8.89
Venezuela (5 brands)	Chimo	17.88 [5.29-30.1]

Stanfill SB, Connolly GN, Zhang L, Jia LT, Henningfield JE, Richter P et al.
Global surveillance of oral tobacco products: total nicotine, unionised nicotine and tobacco-specific N-nitrosamines. Tob Control. 2011

Tobacco & Nicotine Content

- Nicotiana tabacum most common type
- N. rustica common in South Asia, Africa, the Middle East and South Africa. It has higher content of nicotine, minor alkaloids, and tobacco-specific nitrosamines
- N. glauca lacks nicotine but has very high concentrations of anabasine; this plant can be toxic and lethal in some cases.

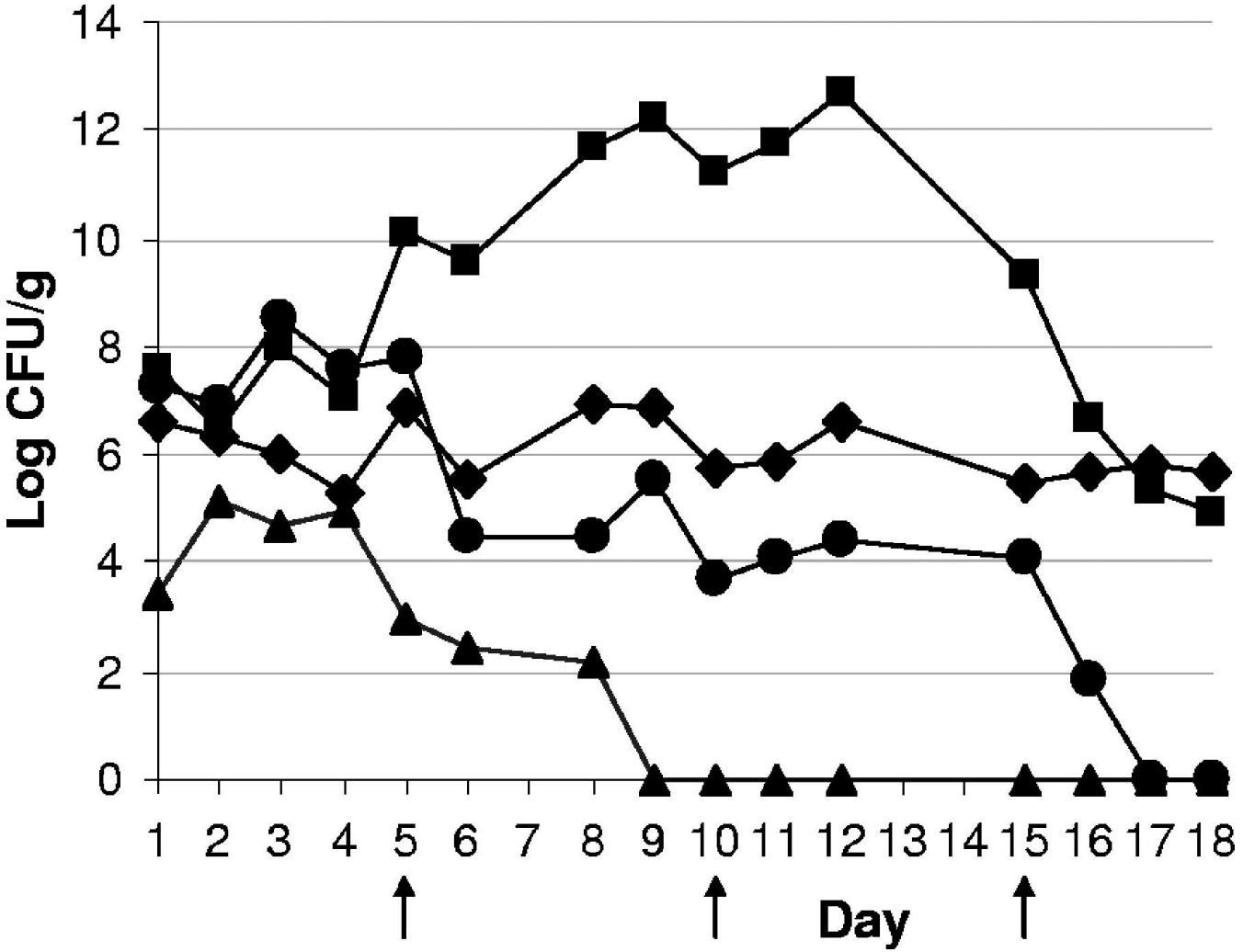
Fire Curing: Higher Levels of Important Toxicants



BAP=Benzo[a]pyrene

Hearn et al. Chemical Analysis of Alaskan Iq'mik Smokeless Tobacco. *Nicotine & Tobacco Research* 2013; doi: 10.1093/ntr/nts270

Microbiological profile of tobacco fermentation as determined by plate counts of major microbial groups



Michele Di Giacomo et al. Appl. Environ. Microbiol. 2007;73:825-837

Applied and Environmental Microbiology

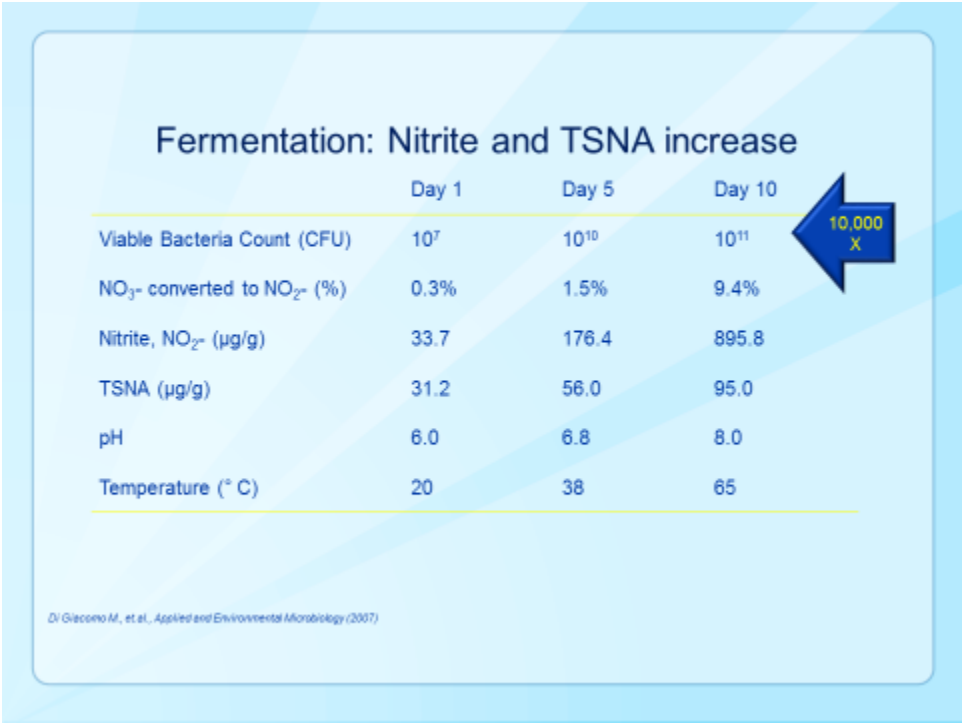
Storage & SLT Toxicants

- Conditions (high temp, high humidity, extended storage) influence TSNA levels
- Storage at ambient temps for 1 year:

  2-fold ↑ in NNN in sun-cured tobacco

  3-fold ↑ in NNN in Burley tobacco
- Rate of increase becomes greater as temperature is increased
- As products “age,” water content can change, leading to bacterial growth, pH and nicotine ↓, nitrosamine levels ↑

Fermentation: Nitrite & TSNA



Regulatory Measures

- Impose product standards
- Apply uniform standards for transnational products
- Reduce appeal and addictiveness

  (? banning flavorings)

Mandated Upper Levels of Toxicants in Smokeless Tobacco

NNN plus NNK	2 microgram per gram of dry weight tobacco
BaP	5 nanogram per gram of dry weight tobacco

The metric for measuring toxicants in smokeless tobacco should be the amount per gram of dry weight of tobacco

WHO TRS 955
The Gothatiek Standard

GOTHIATEK Standard (Swedish Match)

Maximum allowable concentrations of select SLT chemicals.

These reductions have resulted from tracing down contaminations of the SLT processing and manufacturing

In the table below, the limits and the average contents are based on snus, "as is".

Component	Limit	Content 2016 (Conf. interval, 95%)	Component	Limit	Content 2016 (Conf. interval, 95%)
Nitrite (mg/kg)	3.5	1.3 (1.2-1.3)	Cadmium (mg/kg)	0.5	0.28 (0.28-0.29)
NNN+NNK (mg/kg)	0.95	0.39 (0.38-0.40)	Lead (mg/kg)	1.0	0.15 (0.15-0.15)
NDMA (µg/kg)	2.5	<0.6	Arsenic (mg/kg)	0.25	<0.06 (<0.05-0.06)
B(a)P (µg/kg)	1.25	<0.6 (<0.6-0.6)	Nickel (mg/kg)	2.25	0.87 (0.86-0.88)
Aflatoxin B1+B2+G1+G2 (µg/kg)	2.5	<2.1 (<2.1-2.1)	Chromium (mg/kg)	1.5	0.46 (0.45-0.47)
Ochratoxin A (µg/kg)	10	2.3 (2.2-2.3)	Mercury (mg/kg)	0.02	<0.02
Formaldehyde (mg/kg)	7.5	2.3 (2.2-2.3)	Acetaldehyde (mg/kg)	25	6.5 (6.4-6.7)
Crotonaldehyde (mg/kg)	0.75	<0.10	Agrochemicals (mg/kg)	According to the Swedish Match Agrochemical Management Program	Below Swedish Match internal limits

SLT Additives

- Potentiate nicotine effect (e.g. alkaline agents, slaked lime, areca nut) &/or
- Enhance the attractiveness of SLT products (e.g. sweeteners, humectants, salts, flavorants- methyl salicylate, ethyl salicylate, benzaldehyde, citronellol, menthol, nerol, menthone, and caryopyllene most common)

Mean pH

Country	Products	Mean pH
Bangladesh (5 brands)	Gul Powder, Sada Pata, Zarda	7.33 [5.92-9.22]
India (15 brands)	Raja, Gutkha	8.32 [5.22-9.79]
Pakistan (7 brands)	Gutkha, Mawa, Mainpuri, Naswar,	8.44 [7.65-9.14]
Sudan (4 brands)	Toombak	9.30 [7.38-10.1]
Nigeria (2 brands)	Snuff	9.22 [9.02-9.42]
South Africa (9 brands)	Snuff, Snus	7.93 [6.48-10.1]
Sweden (5 brands)	Snus	6.95 [6.61-7.21]
Uzbekistan (1 brand)	Nasway	8.43
Venezuela (5 brands)	Chimo	8.62 [6.98-9.40]

Stanfill SB, Connolly GN, Zhang L, Jia LT, Henningfield JE, Richter P et al.
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Attractiveness

- Taste, smell and other sensory attributes
- Ease and convenience of use
- Cost
- Reputation or image
- Reduced assumed risks and benefits
- Other characteristics of a product designed to stimulate use

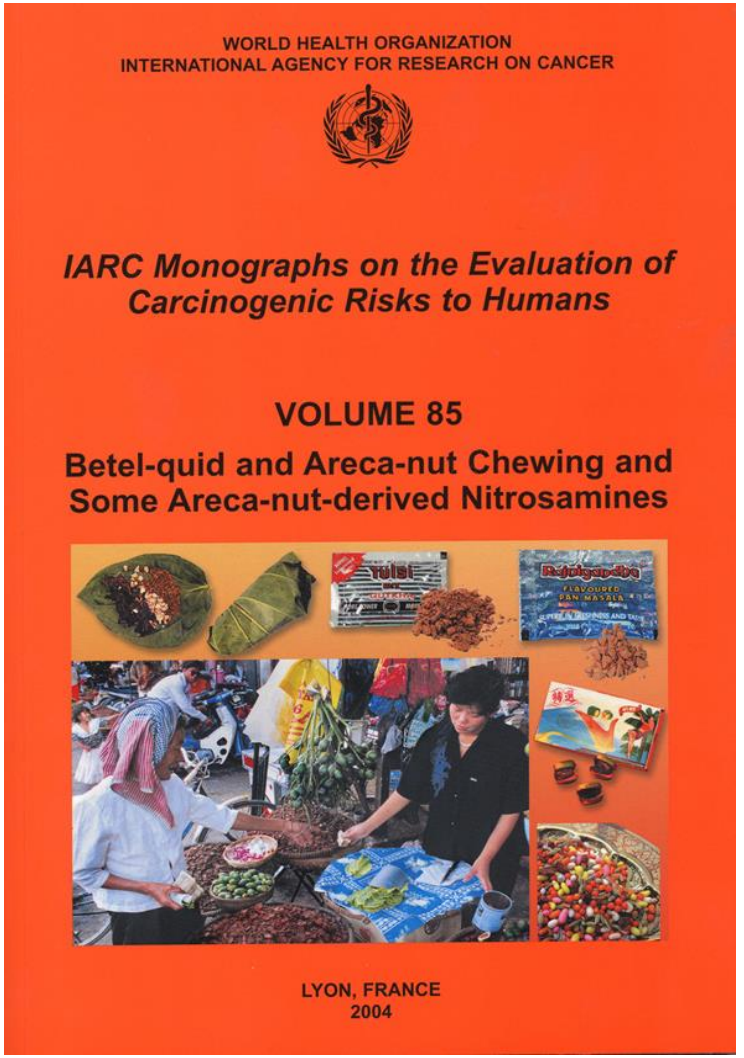
Areca Nut fruit of Areca cathechu

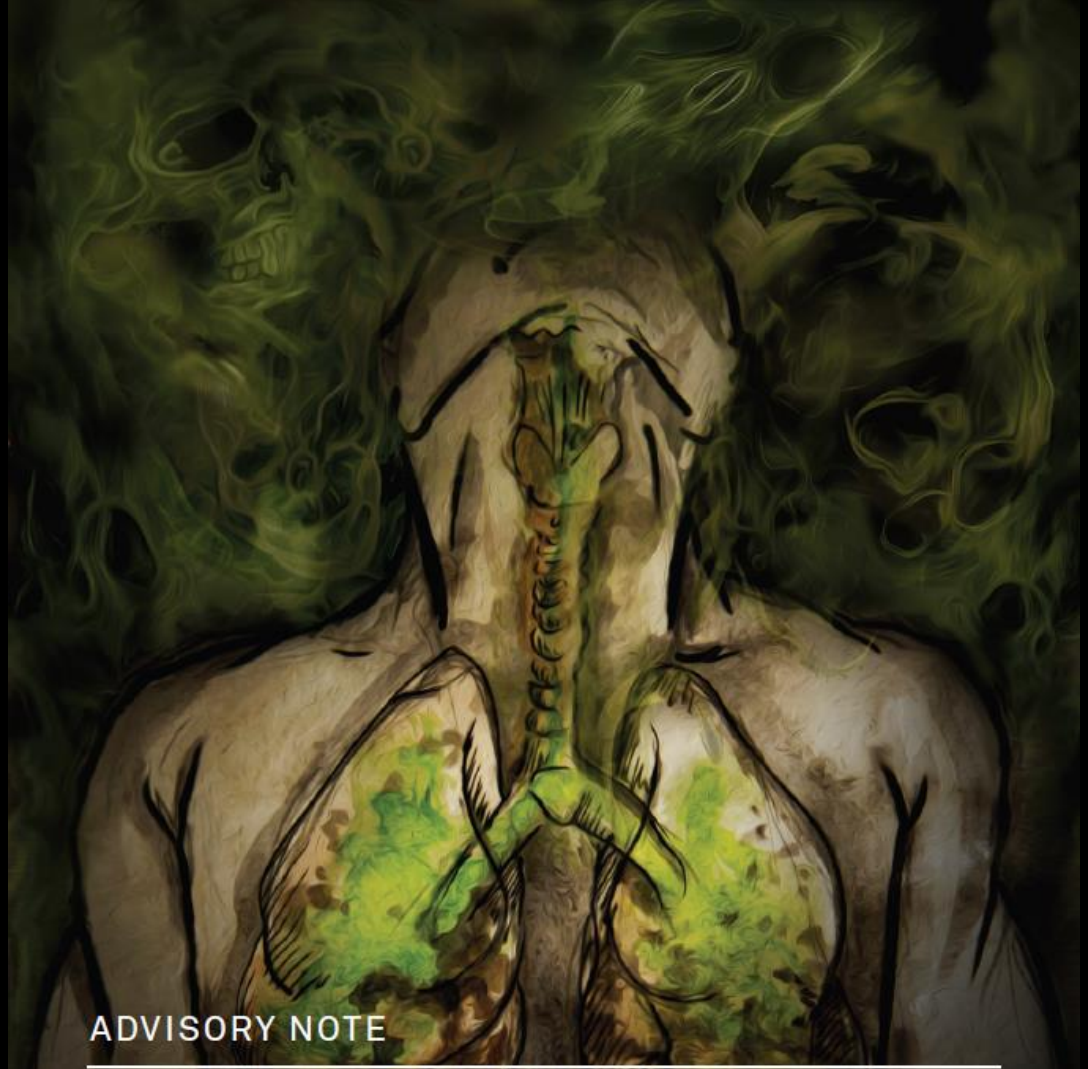
The most active ingredients of the nuts: alkaloids (particularly arecoline) and tannins

IARC Overall Evaluation:

- Betel quid with tobacco is carcinogenic to humans (Group 1)
- Betel quid without tobacco is carcinogenic to humans (Group 1)
- Areca nut is carcinogenic to humans (Group 1)

Group 1 Definition: Sufficient evidence to conclude that it can cause cancer in humans





ADVISORY NOTE

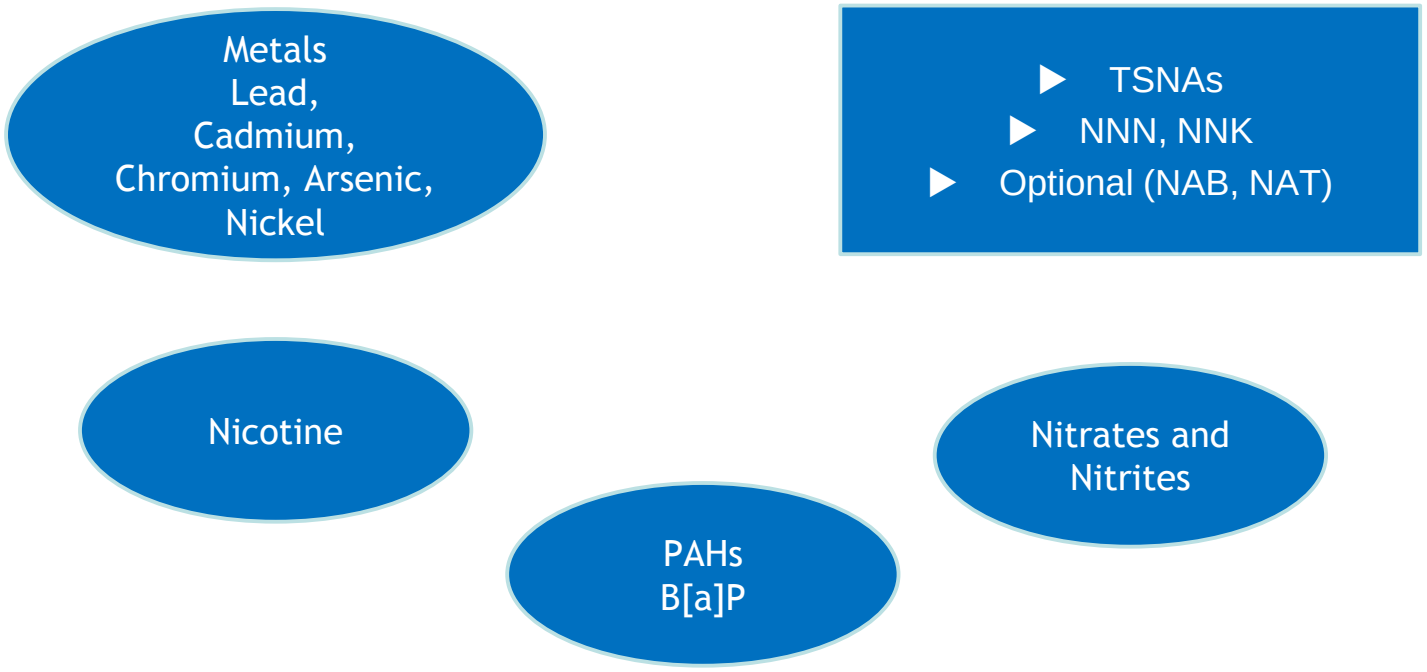
Banning Menthol in Tobacco Products

WHO Study Group on Tobacco Product Regulation (TobReg)

World Health Organization

Chemicals contributing to Toxicity in SLTs

5 Group of Chemicals



TobLabNet: Short and Long Term Strategy

Short Term

Adapt established SOPs to measure chemicals in Smokeless Tobacco
Adapt official methods on food/agriculture products to SLTs
start using the SOP to collect data and share with WHO/national regulatory agency
contents and emissions results to establish (range of limit)

Middle Term (continuous)

setting up an inventory - questionnaire on analytical capabilities, expertise in tobacco testing
Harmonized data reporting to nicotine

Adapt existing SOPs to other tobacco products (ENDS/ENNDS, heat not burn, waterpipe)

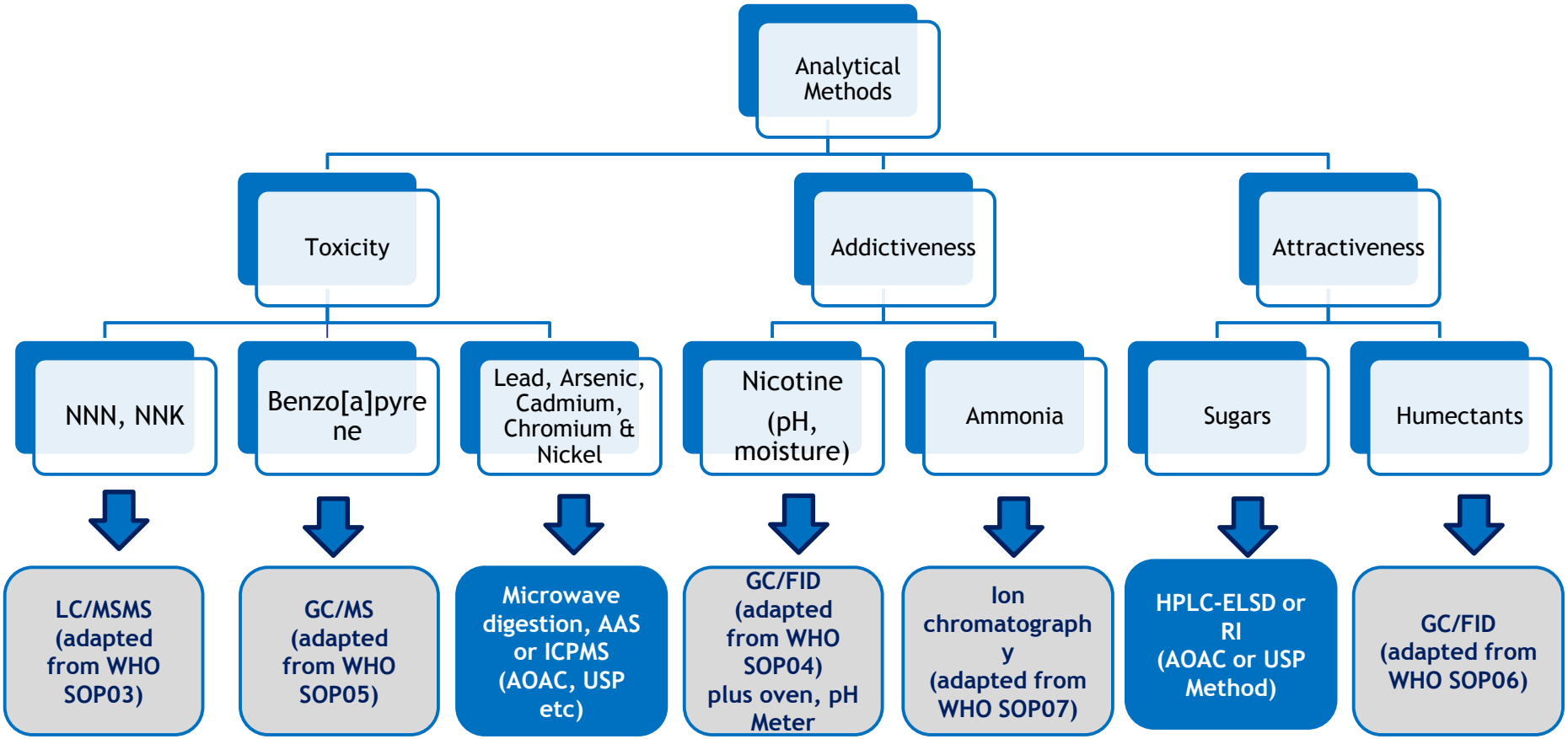
Long Term (continuous)

Recruit more labs to join the verification/validation activities, share experience

Form specialised sub-groups based on expertise within the network (& region) - Knowledge Hub on SLTs, Waterpipe

TobReg Advice
Biomarkers
Ingredients
Toxicants

Analytical Methods for Measuring Chemicals of Interest in SLTs



SOP: Standard Operating Procedure
AOAC: Association of Official Analytical Chemists
USP: United States Pharmacopeia


Tobacco Product Regulation

Key Tobacco Control Policies

- Comprehensive tobacco control programs including monitoring and legislative prevention measures
- Education and awareness efforts on dangers of tobacco use including SLT
- Deep cultural acceptance of these products
- Bans on tobacco advertsing, promotion, and sponsorship
- Raising taxation
- Cessation Programs

The Challenges

- Greater collaboration between the different bodies
- Securing administrative funding for control
- Validation of testing methods
- Universally agreed upon reporting format
- Global data repository
- Overcoming legal challenges by the industry
- Surveillance of novel tobacco products

Conclusions

- Reduce the use of Nicotiana rustica
- Require that tobacco be sun- or flue cured rather than fire- or air cured (lowers PAHs)
- Limit bacterial contamination, which can promote nitrosation and carcinogen formation (lowers nitrosamines)
- Pasteurization to kill bacteria
- Improve storage conditions, such as refrigerating products before sale
- Affix a date of manufacture

Conclusions

- Ban flavorings
- Set manufacturing standards and mandating upper limits for TSNA and benzo(a) pyrene
- Set limits on free nicotine and pH
- Eliminate ingredients such as areca nut and tonka bean which are known to be carcinogenic
- Remove soil and dirt to reduce microbes and metals
- Avoid use of soil amendments that contain heavy metals

Dhaka, Bangladesh, April 2016