World Tobacco Expo

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Hard Science - as a basis for effective regulations

Steve Purkis

Imperial Tobacco Limited

Introduction

- Focus on smoke constituent testing
- Regulatory Drivers
- Need for sound science
- Need for standardisation
- Role of CORESTA and ISO
- Misunderstandings due to data misinterpretation

Regulatory Drivers

- **Health Canada**
  - Testing of 44 smoke emissions + blend constituents + toxicity
- **WHO / TobReg**
  - Development of methodology for 9 priority emissions by 2013
  - Leading to ceilings on smoke constituents
- **FDA**
  - Testing of ~100 smoke constituents in USA market
- **Other Regulatory Authorities e.g. EUTPD**
  - Current ceilings (10/1/10) on tar/nicotine/CO yields

Need for sound science

- Need for scientific basis for choice of smoke constituents
- Need for standardised smoke collection method
- Need for standardised methodology
- Need for “competent and sufficient” numbers of laboratories to carry out collaborative tests to derive variability (tolerance) data
- Recognition of realistic measurement tolerances associated with methods
- Need for a forum to discuss ALL these issues

Need for scientific basis for the choice of 'regulated' smoke emissions

- UK Advisory committees (COT COC COM, 2004).
  - "the analysis of tobacco smoke constituents is not useful in comparing tobacco-based PREPS or predicting risks associated with tobacco smoking".
- TobReg (Scientific Arm of WHO Tobacco Free Initiative, 2008)
  - *"science has not established that reduction of any individual toxicant in machine-measured cigarette smoke, including those proposed in this report, will reduce actual human exposure or disease risk"*
  - *it is not known whether reducing the levels of the high-priority toxicants identified in this report will actually reduce harm or even reduce actual exposure to these harmful compounds"*.

Need for standardised smoke collection method – ISO method

- **Current ISO regime is a standardised method to measure tar, nicotine and other yields for pack labelling purposes**
  - Consistently ranks brands
  - Allows robust comparisons of TNCO yields between laboratories
  - Quantifies tolerance (uncertainty) around measurements
  - Applies smoke collection method to a wide range of smoking machine designs

- **Limitations of capability**
  - Does not predict smoke exposure
  - Cannot predict yield for individuals
  - Method not designed to duplicate human smoking behaviour but…
  - Smoking parameters fall within the normal range observed in smokers

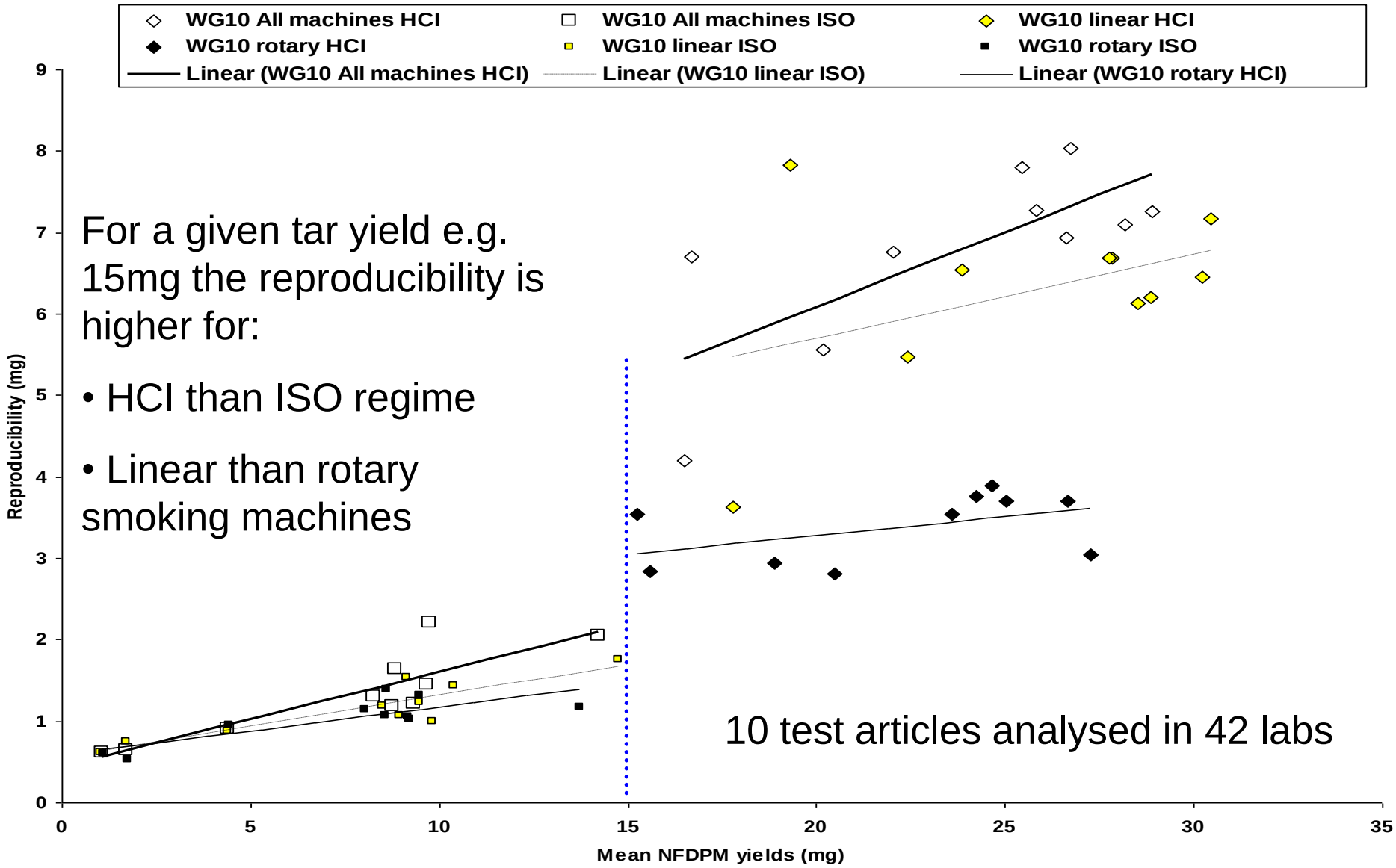
Need for standardised smoke collection method – Intense method?

- **ISO regime has been criticised for giving yields that are:**
  - lower than intake of many smokers and
  - misleading because cigarette design features are over-ridden by many smokers
- **Health Canada Intense Regime has been proposed**

Regime	ISO Method	Health Canada Intense Method
Puff volume (ml)	35	55
Puff Frequency (secs)	60	30
Puff Duration (secs)	2	2
Vent blocking %	0	100

- **Flawed Approach**
  - Assumes that smokers vent block 100% of ventilation holes
  - Assumes that smokers smoke to a constant nicotine intake
  - Gross over-estimation of smoke intake by most smokers
  - Worse correlation to human smoking than ISO (Hammond, 2007)
  - Will it drive future cigarette designs towards those that fit with these flawed assumptions rather than those that reduce human exposure?

Increased data variability between laboratories using the intense method



For a given tar yield e.g. 15mg the reproducibility is higher for:

- HCI than ISO regime
- Linear than rotary smoking machines

10 test articles analysed in 42 labs

Need for standardised smoke collection method – Intense method?

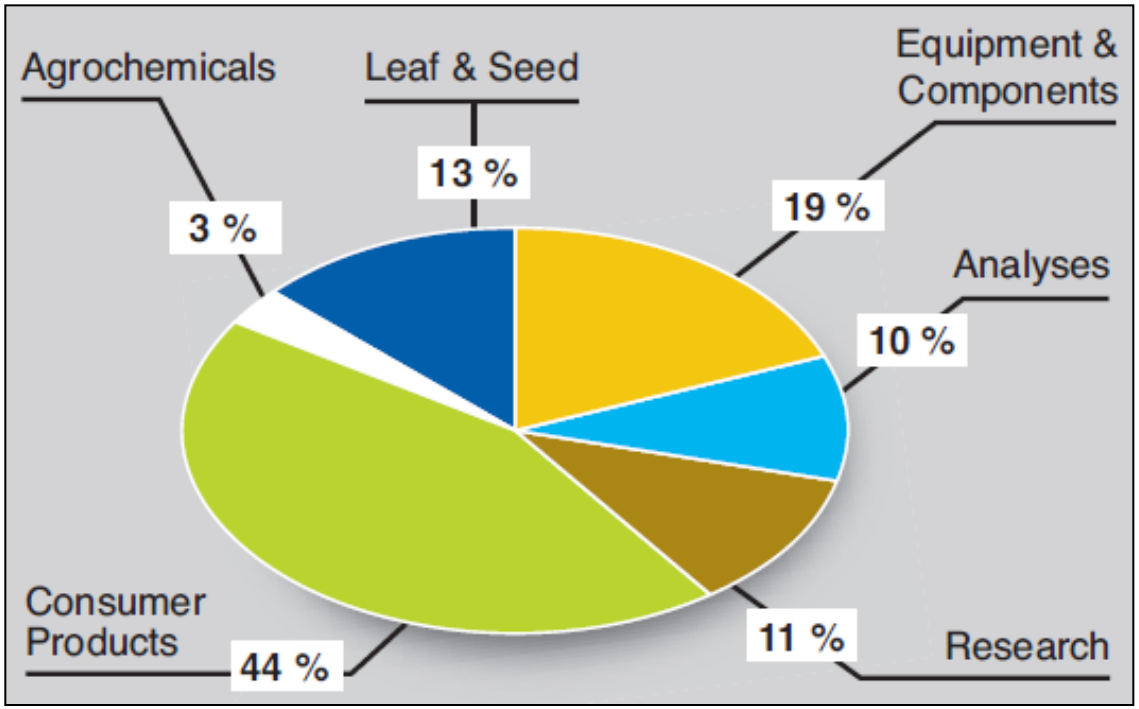
- **Health Canada Intense regime gives less robust yield data than the ISO regime**
  - Higher tar variability between laboratories than the ISO regime
  - Significant yield differences observed between the linear and rotary smoking machines for water and NFDPM – especially for water
    - However, significant differences also within any one machine type
  - Will any other analytes behave like water?
- **Greater numbers of apparent non-compliances due to measurement variability?**
  - potentially interpreted as lack of control by manufacturers to meet regulatory limits

Need for collaborative studies

- Many organisations involved in collaborative studies
  - Participation is a requirement of ISO 17025 accreditation
- **CORESTA**
  - Various studies (as discussed later)
  - Including TNCO and other smoke constituents under ISO / HCI regimes
- **ISO**
  - Working Group 10 – TNCO under ISO and HCI regimes (35 labs)
- **European Collaborative Study (EUCS)**
  - TNCO under ISO regime
- **Asian Collaborative Study (ACS)**
  - TNCO under ISO regime
- **TobLabNet**
  - 9 priority smoke constituents under ISO and HCI regimes + some blend constituent methods

CORESTA Membership

- 178 members currently
- From manufacturers / regulators / universities / suppliers etc
- Further information on CORESTA can be found on their website
  http://www.coresta.org/



There are 57 active CORESTA Recommended Methods

CORESTA collaborative studies

Smoke Science Study Group

- Smoke constituents under ISO and HCI regimes (Special Analytes SG)
- Ames / NRU / Micronucleus toxicity (*In-vitro* Toxicity Task Force)
- “Yield-in-use” filter studies (Smoking Behaviour SG)
- Acrolein biomarker (Biomarkers SG)

Product Technology Study Group

- Blend constituents (Routine Analytical Chemistry and Smokeless SGs)
- TNCO and LIP (Routine Analytical Chemistry SG)
- Cigar smoking regime for TNCO (Cigar smoking methods SG)
- Agrochemicals (Agrochemical Analysis SG)
- Cigarette permeability and pressure drop (Physical Test Methods SG)

Need for standardised methodology for other smoke constituents

- Evaluation of available methods
- Does the method trap all of the smoke constituent?
- Does the method measure all of the trapped constituent?
- Does the constituent degrade after trapping and before measurement
- Does the smoking machine set-up cause some material to behave differently
- Need for collaborative studies to obtain mean, repeatability (‘r’) and reproducibility (‘R’) data

CORESTA - Smoke constituents

Smoke constituent	No. of data sets	Reference	Test article	Units	Mean	R	R %
NFDPM	60	CORESTA, study 2009	CM6	mg/cig	14.3	1.8	12
Nicotine			CM6	mg/cig	1.4	0.13	9
CO			CM6	mg/cig	14.8	1.64	11
B[a]P	13	CRM 58	2R4F	ng/cig	7.3	2.5	35
NNN	9	CRM 63	2R4F	ng/cig	146	32	22
NNK			2R4F	ng/cig	141	44	31
NAT			2R4F	ng/cig	143	64	44
NAB			2R4F	ng/cig	17	11	64
1,3-butadiene	20	CRM 70	3R4F	µg/cig	41	30	71
isoprene			3R4F	µg/cig	362	134	37
acrylonitrile			3R4F	µg/cig	8.6	3.6	42
benzene			3R4F	µg/cig	42	15	37
toluene			3R4F	µg/cig	65	31	48
formaldehyde	15	CRM ##	3R4F	µg/cig	18.8	13.0	69
acetaldehyde			3R4F	µg/cig	538	177	33
acetone			3R4F	µg/cig	206	99	48
acrolein			3R4F	µg/cig	47.6	23.7	50
propionaldehyde			3R4F	µg/cig	39.8	15.7	39
crotonaldehyde			3R4F	µg/cig	12.1	14.4	119
2-butanone			3R4F	µg/cig	48.0	30.0	63
butyraldehyde			3R4F	µg/cig	26.9	12.3	46

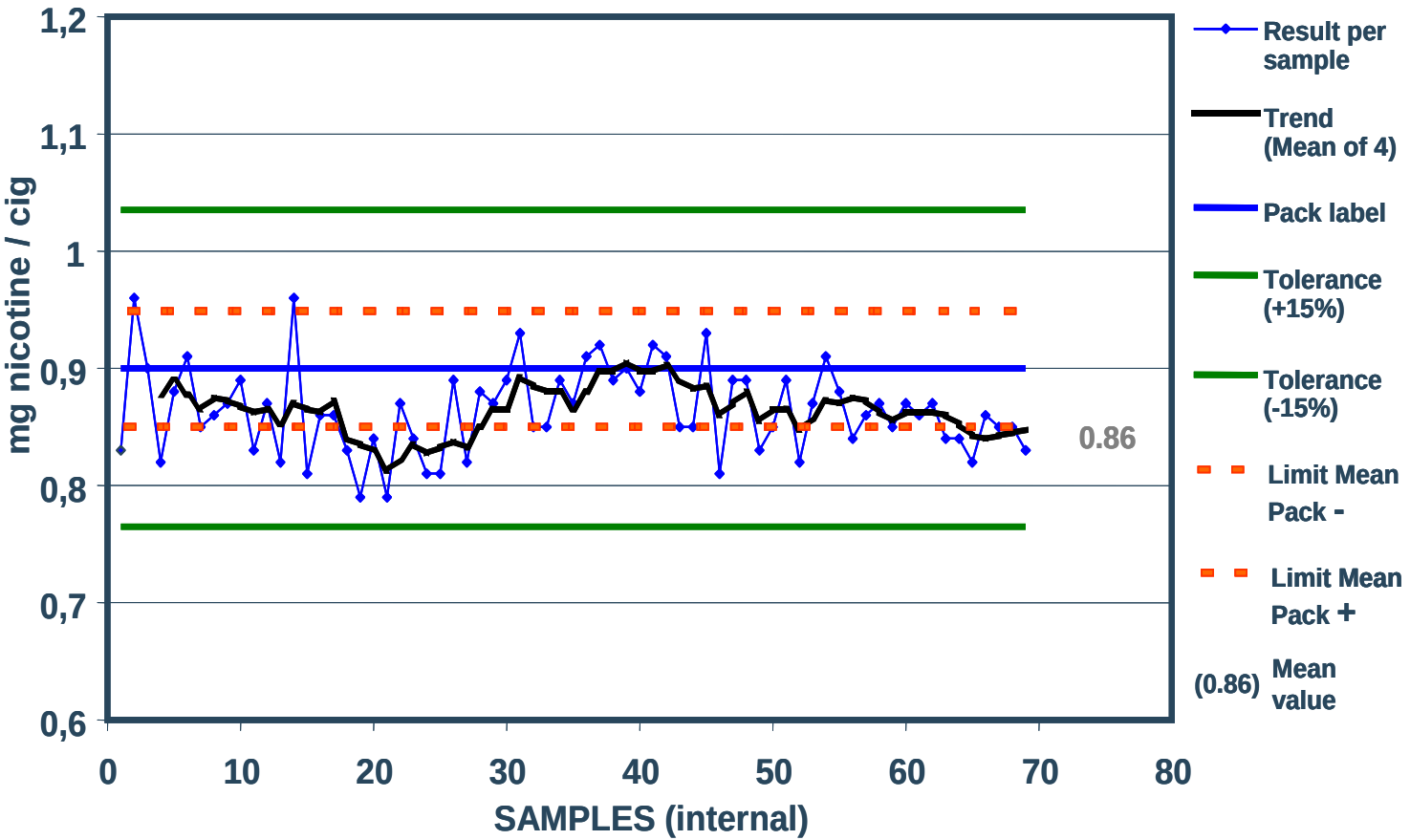
- Reproducibility expressed as a % mean (R%) for TNCO is the region of the 15% tolerance given in the ISO standard
- Tolerances for other smoke constituents will need to be higher
  - Or high number of apparent non compliances will be found

BaP CRM taken forward to ISO 22634, 2007

All data obtained under the ISO smoking regime

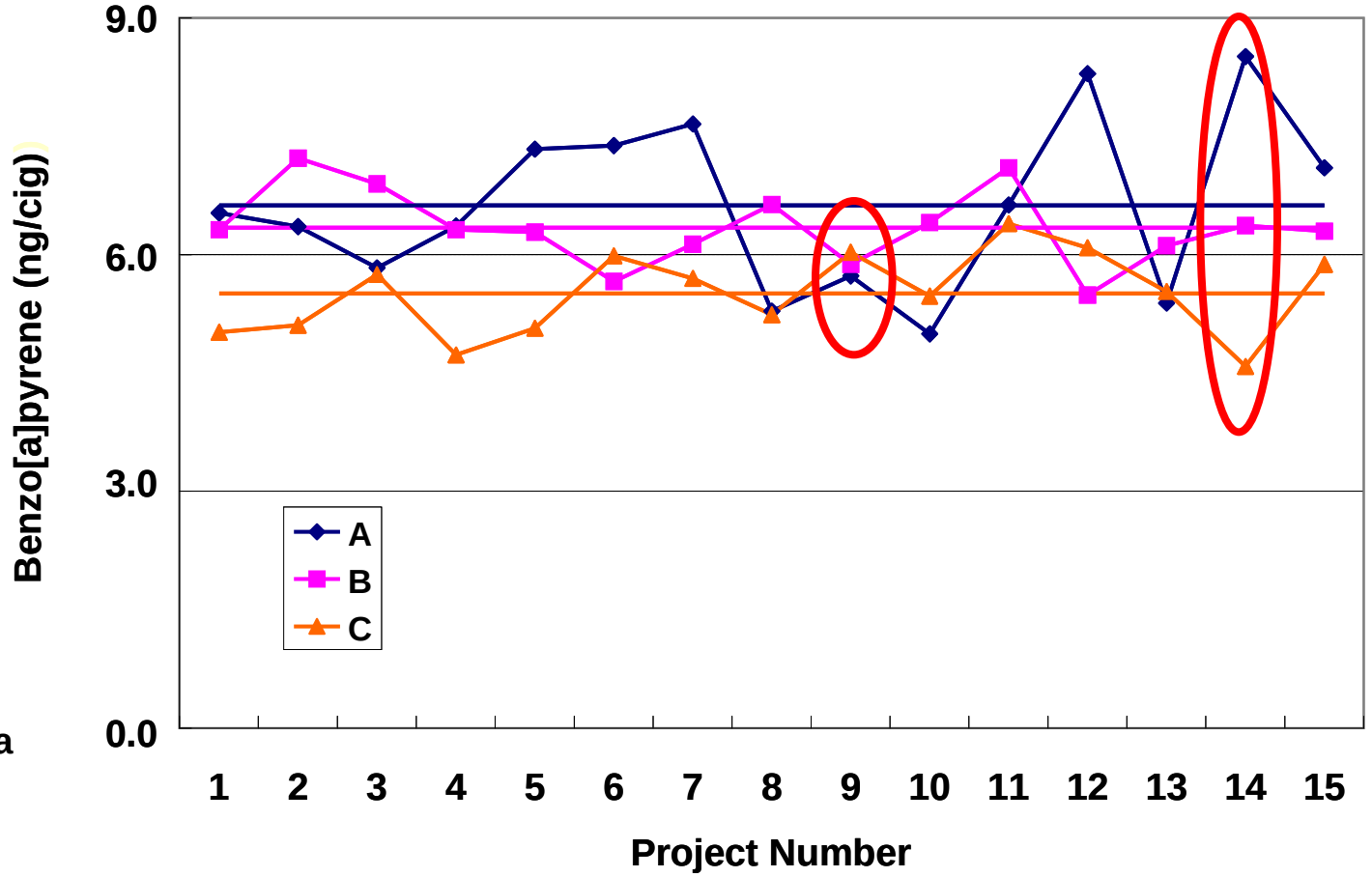
Tolerances and control charts

- Yields are controlled by the making specification. However, yields can fluctuate during production and this is a normal phenomenon.
- One point in time measurements in the one laboratory may fluctuate around mean (0.86 mg) but yields are well within the 15% ISO tolerance.



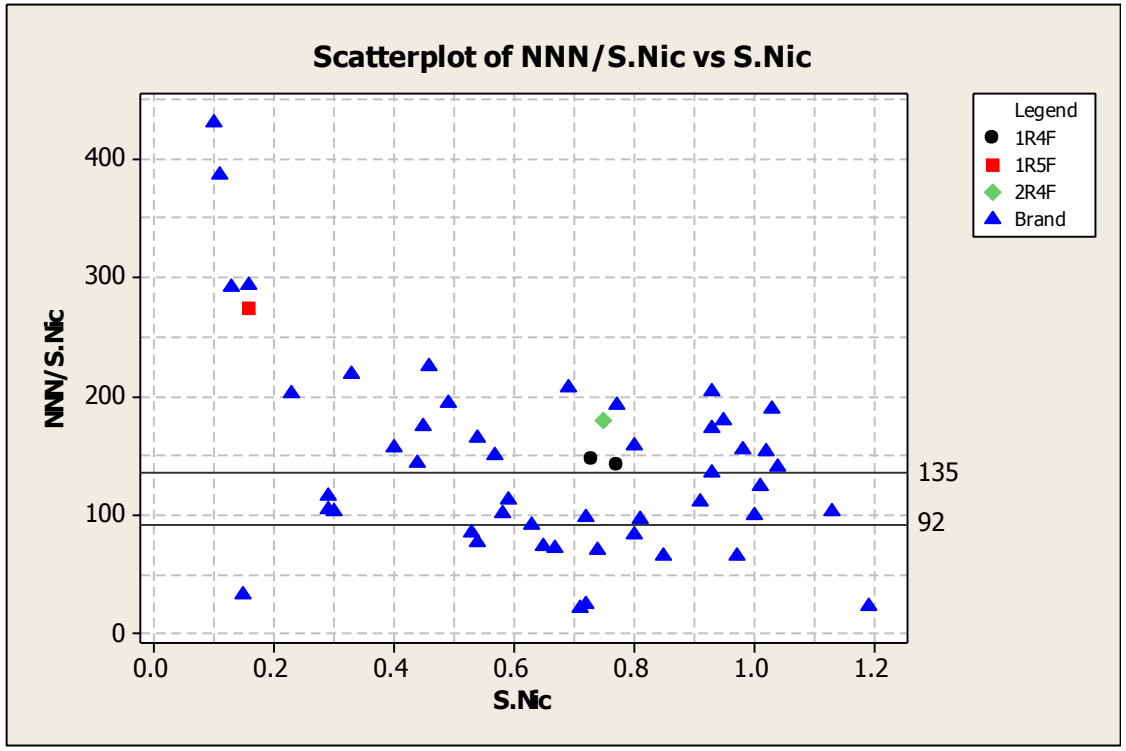
B[a]P variation over time in 3 laboratories

- B[a]P yields determined on 2R4F reference cigarette run over 4 years.
- The lowest ratio between the highest and lowest yield was 5 % in project 9 and the highest ratio at 86 % in project 14.
- Conclusions drawn from one point in time studies may not be robust



Hyodo et al, data presented at CORESTA, 2006

NNN / Nicotine ratios

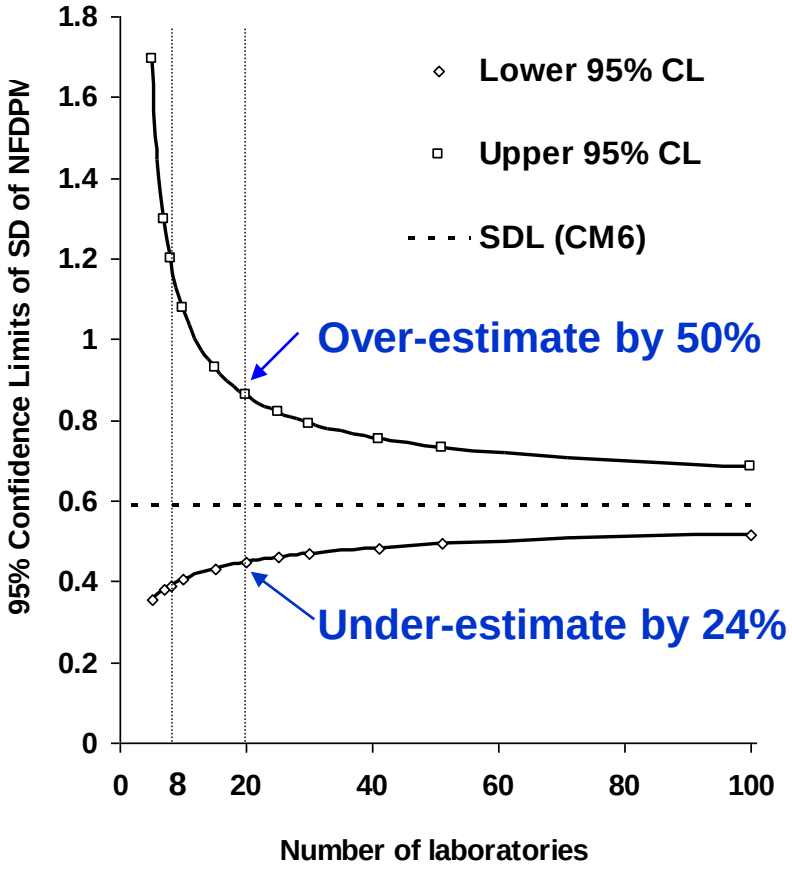


Data on PM brands (Counts et al, 2005) used by TobReg

If this were a market study then all products above 135 (median value) would have to be removed from the market

- Applying upper limits of reproducibility (R) from the NNN CORESTA CRM 63 for 2R4F under ISO smoking then:-
- All products with ratio above 92 are subject to “apparent” non-compliance
- Only 26% of brands would be acceptable (with 95% confidence) with no disputes over “apparent” non compliance.
- Most lower delivery products must be removed!! – is this really a “good” approach?– further work being done through CORESTA

Number of labs in collaborative study



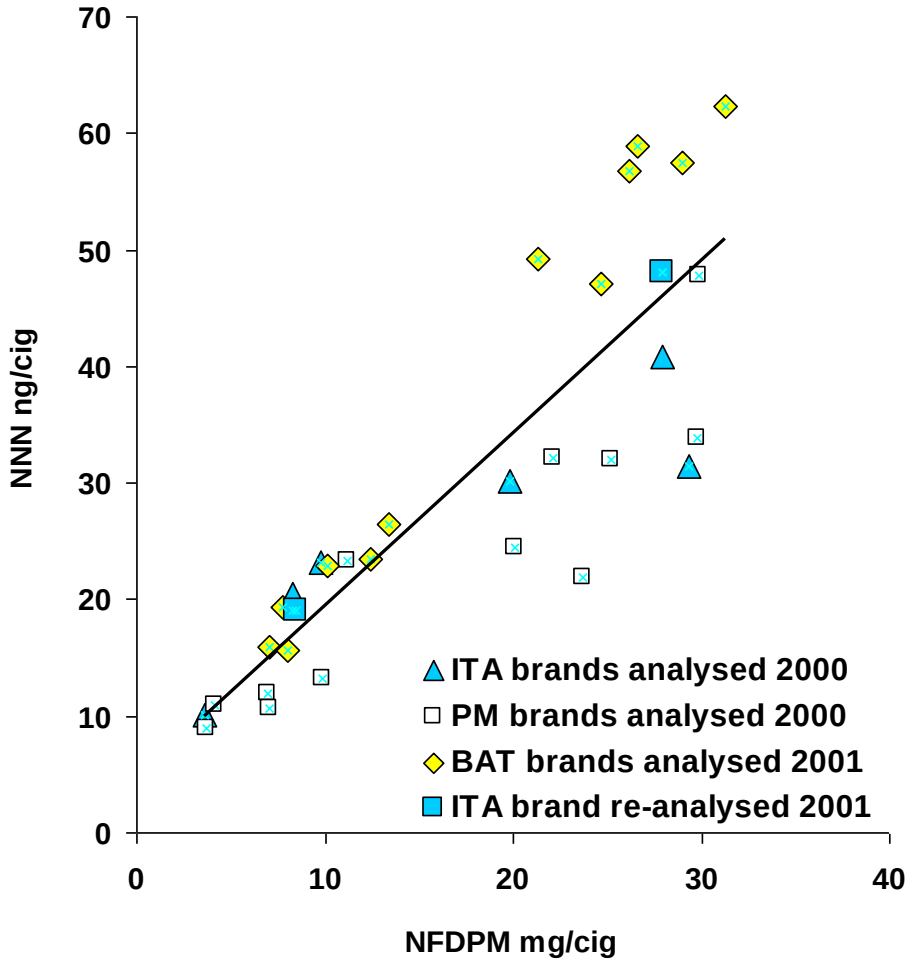
NFDPM Standard deviation of CM6 from the 2009 CORESTA study

- ISO 5725 analysis applied

- For 20 participating laboratories, the standard deviation could be over-estimated by almost 50 % or under-estimated by 24 %.
- Using only 8 laboratories could over-estimate the standard deviation by 100 % or under-estimate by 66 %.
- Around 20 laboratories is necessary to obtain a realistic and robust estimate of the reproducibility R.

Misunderstandings arising from the Australian benchmark data

15 brands measured under ISO and HCI regimes for 44 smoke constituents



- 6 PM and 3 ITA brands measured at one point in time
- 6 BAT and one ITA brand measured at a later point in time
- Observed differences were wrongly interpreted as differences in blends (King and Borland, 2007)
- The reference cigarette in the testing laboratory for both points in time demonstrated the same apparent differences.
- NNN example given here
- **Misinterpretation of blend "differences" due to measurement variability in one laboratory over time**

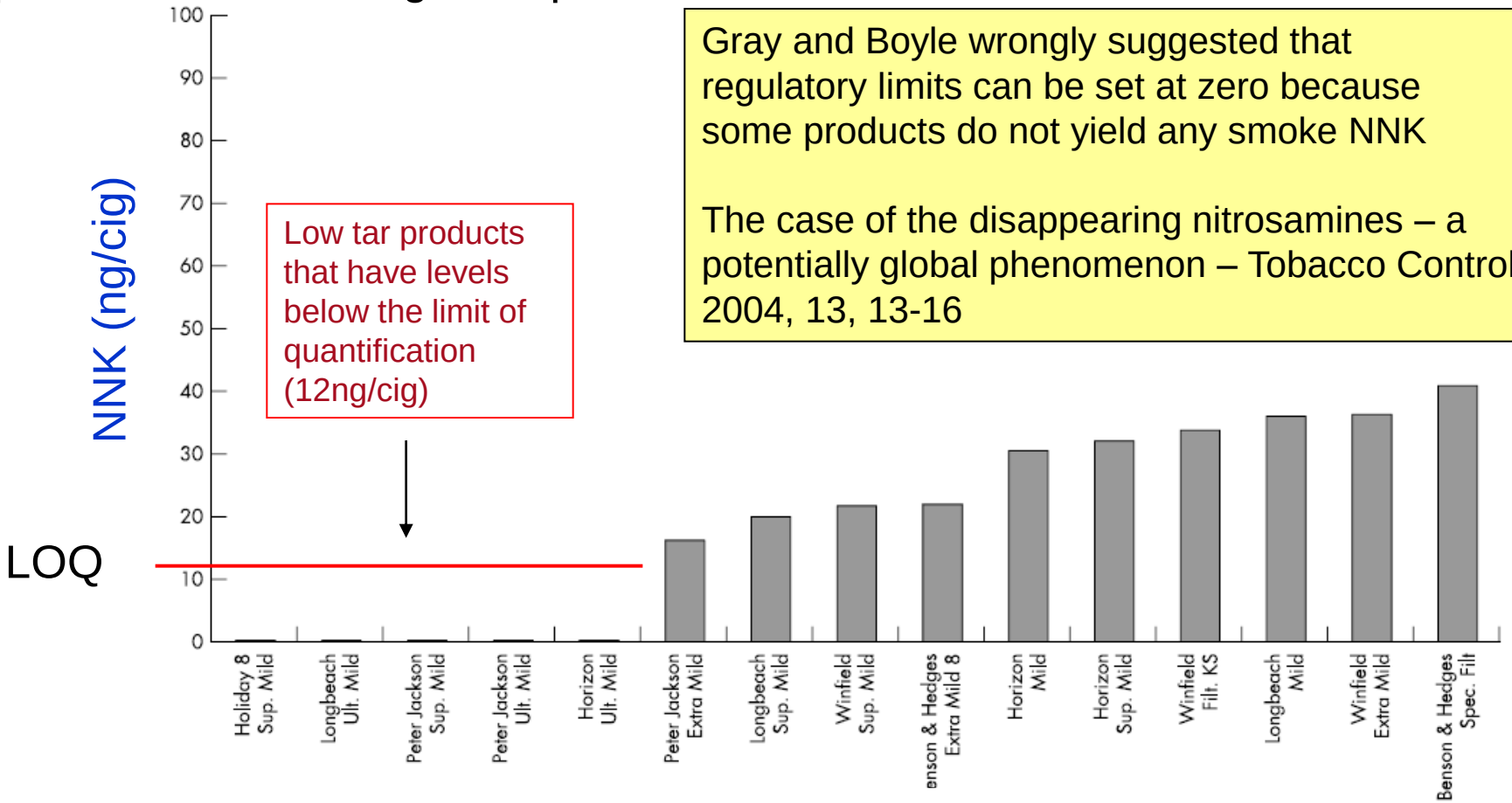
  – DIALOGUE required.

Misunderstandings arising from the Australian benchmark data

Yield misinterpretation due to measurements being below the limits of quantification – dialogue required

Gray and Boyle wrongly suggested that regulatory limits can be set at zero because some products do not yield any smoke NNK

The case of the disappearing nitrosamines – a potentially global phenomenon – Tobacco Control 2004, 13, 13-16

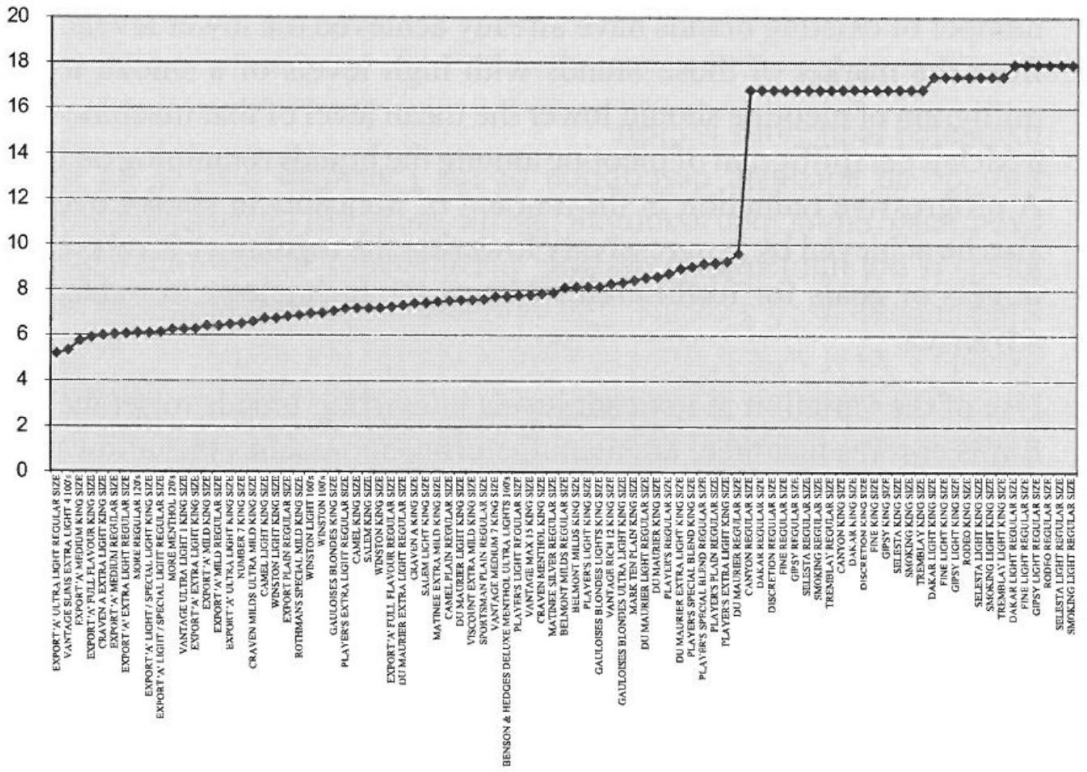


15 commercial brands in Australia

Canadian data from TobReg (2008)

- Some products appear to have elevated BaP/Nicotine ratios compared to others – dialogue required
  - Unclear if this is product design related or due to measurement variability ?

BaP/Nicotine Ratio



Brand

Conclusions

- Future tobacco product regulation and measurement methods need to be based on **SOUND SCIENCE**.
- Various organisations can propose methods for ISO standardisation after they have been through careful **VALIDATION**
  - **SUFFICIENT** numbers of labs should be involved in **COLLABORATIVE** studies
- ISO **STANDARDISATION** process allows worldwide members to collectively develop a sound methodology useful for regulation.
- Manufacturers and regulators alike need to understand the limitations of methodology used to measure smoke yields.
  - …. and then set **REALISTIC TOLERANCES**.
- A **FORUM** for regulators and manufacturers to discuss methodological issues
  - to allow any apparent yield differences due to methodology to be discussed at an early stage.

Related papers

- Intorp, M., Purkis S.W., Whittaker M.W., Wright W., 2009. Determination of “Hoffmann analytes” in cigarette mainstream smoke. The CORESTA 2006 collaborative study; Beiträge Tabakforsch. Int. 23, 161-202.
- Purkis S.W., 2009. Analysis of the data variability in the Australian benchmark study 2000-2001; Beiträge Tabakforsch. Int. 23(5), 334-336.
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- Purkis, S.W., Mueller, C., Intorp, M., Seidel, H., 2010. The influence of cigarette designs and smoking regimes on vapour phase yields. Beitr. Tabakforsch. Int. 24(1), 33-46.
- Purkis, S.W., Troude, V., Duputié, G., Tessier, C., 2010. Limitations in the characterisation of cigarette brands using different smoking regimes. Reg. Toxicol. Pharmacol. 58, 501-515.
- Purkis, S.W., Meger, M., Wuttke, R. 2011. A review of current smoke constituent measurement activities and aspects of yield variability. Reg. Toxicol. Pharmacol. In press

Thank you for your attention !

http://www.imperialtobaccoscience.com/