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The UK Smoke Constituents Testing Study. Summary of Results and Comparison with Other Studies*

by

Evan Gregg[1], Colin Hill[2], Mike Hollywood[3], Malachy Kearney[3], Kevin McAdam[4], David McLaughlin[3], Steve Purkis[5], and Mark Williams[4]

[1]*Consultant to the Tobacco Manufacturers' Association, Burwood House, 14/16 Caxton Street, London, SW1H 0ZB*
[2]*Consultant to Imperial Tobacco Limited*
[3]*Gallaher Limited, Group R&D, 201 Galgorm Road, Lisnafillan, Ballymena BT42 1HS*
[4]*British American Tobacco, R&D Centre, Millbrook, Southampton SO15 8TL*
[5]*Imperial Tobacco Limited PO Box 525, Southville Bristol BS99 1LQ*

SUMMARY

At the request of the UK Department of Health, samples of 25 commercial UK cigarette brands were provided to LGC Ltd[a] for smoke analysis. The brands reflected a high market share (58% in July 2001) and included a wide range of blend and product styles manufactured and imported into the UK.

The main objectives were to determine the yields, under International Organisation for Standardisation (ISO) smoking conditions, of 44 smoke constituents in mainstream smoke, and to establish the functional relationships between the smoke constituent yields and nicotine-free dry particulate matter (NFDPM or "tar") and CO yields. A third objective concerned possible variation in yields of smoke constituents associated with cigarette design features.

All smoke constituent yields gave statistically significant positive correlations with NFDPM yield; however, the volatile constituent yields showed a stronger association with CO yield. Twenty-two out of 1000 brand-analyte results were identified as regression outliers, reflecting three well-known and previously documented observations: 1) differences in the relative yields of nitrogen-containing constituents due to tobacco blend style; 2) differences in constituent yields between filtered and unfiltered ("plain") cigarettes; and 3) measurement uncertainty. In a normalised model, excluding regression outliers, the overall correlation between NFDPM yield and all other smoke constituent yields was $r = 0.87$ ($R^2 = 0.76$), suggesting a minor role of other design features on constituents yield variability. This was confirmed by the application of multiple regression analysis to the data.

A subset of five brands, retested at another laboratory, gave between-laboratory differences in mean constituent yields of as much as 2.5-fold. Consideration of these results, other likely sources of analytical variation in this study and a review of other studies, clearly indicates that any tolerance values to be associated with individual smoke constituent measurements will be greater than those for NFDPM, and in some cases, much greater.

Consistent with the reported results from other large studies it is concluded that, under ISO smoking conditions, smoke constituent yields are largely predictable, if NFDPM and CO yields are known, for a standard cigarette. Given these observations and the likely limitations of analytical determination, the need for routine measurement of smoke constituent yields, other than NFDPM, nicotine or CO, on standard cigarettes, is questionable. [Beitr. Tabakforsch. Int. 21 (2004) 117–138]

ZUSAMMENFASSUNG

Auf Ersuchen des britischen Gesundheitsministeriums wurden LGC Ltd. Proben von 25 gängigen britischen Zigarettenmarken für Rauchanalysezwecke zur Verfügung gestellt. Die untersuchten Zigarettenmarken haben einen hohen Marktanteil (58% im Juli 2001) und umfassen ein breites Spektrum an Geschmacksrichtungen und Produktvariationen, die in Großbritannien produziert bzw. dorthin importiert werden.

Hauptzielsetzung war es, unter den von der Internationalen Organisation für Normung (ISO) festgelegten Standardbe-

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[a] In December 2001, during the course of this study, Molins PLC acquired the tobacco section of LGC Limited, which now trades as Arista Laboratories Europe. To avoid confusion, the name LGC has been retained throughout this report.

dingungen die Abrauchwerte für 44 Bestandteile des Hauptstromrauchs zu ermitteln und deren funktionalen Zusammenhang mit dem nikotinfreien Trockenkondensat (NFDPM, Kondensat) und dem Kohlenmonoxid (CO) zu bestimmen. Ein weiteres Ziel umfasste die Untersuchung möglicher Variationen in der Menge der Rauchbestandteile, die im Zusammenhang mit den Produkteigenschaften der Zigaretten stehen.
Die Werte aller Rauchbestandteile zeigten eine statistisch signifikante positive Korrelation mit den Kondensatwerten, die flüchtigen Rauchbestandteile hingegen standen in stärkerem Zusammenhang mit den CO-Werten. Bei 22 der 1000 Analyseergebnisse handelte es sich um statistische Ausreißer, die drei bekannte und bereits dokumentierte Beobachtungen widerspiegeln: 1) Unterschiede in den relativen Werten der stickstoffhaltigen Bestandteile in Abhängigkeit von der jeweiligen Tabakmischung; 2) Unterschiede in den Werten der Rauchbestandteile von Filterzigaretten und filterlosen Zigaretten; und 3) Messunsicherheiten. In einem normalisierten Modell und unter Ausschluss statistischer Ausreißer beträgt der Gesamtzusammenhang zwischen den Kondensatwerten und den Werten aller übrigen Rauchbestandteile $r = 0.87$ ($R^2 = 0.76$); dies deutet darauf hin, dass andere Konstruktionsmerkmale einen eher unbedeutenden Einfluss auf die Variabilität der Rauchbestandteile haben. Diese Vermutung wurde durch eine multiple Regressionsanalyse bestätigt.
Eine Auswahl von fünf Zigarettenmarken, die in einem anderem Labor nochmals getestet wurden, ergab eine bis zu 2,5fache Abweichung der Mittelwerte zwischen den Labors. Eine Untersuchung dieser Ergebnisse und möglicher weiterer Ursachen der analytischen Abweichungen sowie die Einbeziehung diverser anderer Studien zeigt deutlich, dass der Toleranzbereich der einzelnen Rauchbestandteile höher ist als derjenige für Kondensat, in einigen Fällen wesentlich höher.
In Übereinstimmung mit den Ergebnissen anderer umfassender Studien kann die Schlussfolgerung gezogen werden, dass die Werte der Rauchbestandteile für Standardzigaretten unter ISO Abrauchbedingungen größtenteils voraussagbar sind, sofern die Kondensat- und CO-Werte bekannt sind. Angesichts dieser Beobachtungen und den möglichen Grenzen analytischer Untersuchungen ist es fraglich, ob die routinemäßige Messung anderer Rauchbestandteile als die von Kondensat und CO in Standardzigaretten notwendig ist. [Beitr. Tabakforsch. Int. 21 (2004) 117–138]

RESUME

Sur demande du Ministère britannique de la Santé publique, des échantillons de 25 marques de cigarettes du marché britannique ont été fournies au laboratoire LGC Ltd. pour analyse de la fumée. Les marques représentent une part importante (58% en Juillet 2001) du marché britannique et couvrent un large éventail de mélanges de tabac et de conceptions des cigarettes fabriquées et importées en Grande-Bretagne.
L'objectif principal de l'étude était de doser le rendement en 44 composants dans le courant principale de la fumée en conditions de fumage normalisées ISO (International Organisation for Standardisation) et d'établir des corrélations entre les rendements en composants de la fumée et le rendement en matière particulaire anhydre et exempte de nicotine (MPAEN ou goudron) et en monoxyde de carbone (CO). Un troisième but était d'examiner des variations possibles des rendements en composants de la fumée associés aux conceptions des cigarettes.
Tous les rendements des composants de la fumée présentent des corrélations positives et significatives avec le rendement en MPAEN, et les composants volatils sont plus fortement corrélés avec le rendement en CO. Vingt-deux des 1000 données obtenues ont été identifiées comme données aberrantes, reflétant trois observations bien connues et déjà documentées: 1) des différences dans les rendements relatifs en composants azotés associés au mélange du tabac; 2) des différences dans les rendements en composants entre les cigarettes avec ou sans filtres; et 3) l'incertitude de la mesure. Dans un modèle normalisé à l'exclusion des données aberrantes, la corrélation générale entre le rendement en MPAEN et le rendement en tous les autres composants de la fumée est de $r = 0.87$ ($R^2 = 0.76$), suggérant que d'autres caractéristiques de la conception des cigarettes sont de moindre importance pour la variabilité des rendements en composants de la fumée d'une cigarette. Ceci a été confirmé par une analyse de régression multiple.
Un sous-échantillon de cinq marques, testé de nouveau dans un autre laboratoire, révèle des différences entre les laboratoires dans les rendements moyens en composants d'une variation d'un facteur de 2.5. La considération de ces résultats et d'autres sources de variation statistique potentielles ainsi que l'examen d'autres études indiquent clairement que la marge de tolérance des mesures de composants singuliers de la fumée est plus grande que celle pour le MPAEN et, dans certains cas, beaucoup plus grande.
En accord avec les résultats d'autres études importantes on a conclu que, dans les conditions de fumage normalisées ISO, les rendements en composants de la fumée d'une cigarette standard sont largement prévisibles, si les rendements en MPAEN et en CO sont connus. Etant donné ces observations et les limites probables du dosage analytique, la question se pose, pour des cigarettes standard, de la nécessité de mesures de routine des rendements en composants de la fumée, autre que le MPAEN, la nicotine et le CO. [Beitr. Tabakforsch. Int. 21 (2004) 117–138]

INTRODUCTION

Background

The chemical composition of the smoke evolved from a burning cigarette has been studied for many years and certainly since the 1950s (1). As measurement and instrumentation techniques have progressed and become more sensitive, the list of chemicals detected in mainstream smoke has grown. By 1986, approximately 4000 chemicals had been reported in mainstream and sidestream smoke (2) and this number has continued to increase (3,4,5).
Since the 1970s a group at the American Health Foundation, led by DIETRICH HOFFMANN, has catalogued and published a list of "biologically active substances in cigarette smoke" (6). In 1988, the UNITED KINGDOM INDEPENDENT

SCIENTIFIC COMMITTEE ON SMOKING AND HEALTH reported the yield of some of these chemicals from cigarette brands then on sale in the UK, based on a market survey approach (7). The analyses of these smoke constituents was conducted by LGC, who subsequently published other papers comparing more of these smoke constituents from UK cigarette brands, including differences between blend styles (8,9,10).

More recently, there has been renewed interest in the analysis of some of these smoke constituents. One approach has been to seek functional relationships between the yield of nicotine-free dry particulate matter (NFDPM or "tar") or nicotine or carbon monoxide and the yield of other smoke constituents in "benchmark studies" such as those performed in the US State of Massachusetts (11) and in Canada (12). In these studies, a minimum set of 25 cigarette brands from a single market was selected and analysed for 44 specified smoke constituent yields. Both studies included design features widely used in cigarette manufacture (presence or absence of a filter, the level of filter ventilation, cigarette circumference and length, paper porosity and the use of menthol) within a single tobacco blend style available in each market. A similar study was performed in Australia, using the methods published by Health Canada and the same testing laboratory (13).

Study protocol

In the summer of 2001 the UK Department of Health (DH) asked the UK-based Tobacco Manufacturers' Association (TMA) member companies to fund a UK smoke constituent study and the DH appointed LGC Limited to carry out the analyses. The DH also specified a range of cigarette design features to be included. The protocol was agreed between the DH and the contract laboratory, prior to the TMA assuming a management role for the study. The full study protocol is available at www.the-tma.org.uk and the main features only are summarised herein.

From the outset, the UK study was intended as a single point-in-time "snapshot" analysis of smoke constituents and the two main aims were described as follows:

- To determine the yield ratings of 44 selected smoke constituents in mainstream smoke under International Organisation for Standardisation (ISO) smoking conditions for selected cigarette brands that were typical of all blend styles sold in the UK.
- To establish the functional relationships between smoke constituent yields and NFDPM yield and between volatile smoke constituent yields and carbon monoxide yield.

An additional aim was to investigate the possible contribution of cigarette design features to any variation in specific smoke constituent yields.

Study scope and limitations

Summary results from the UK Smoke Constituents Testing Study and its interpretation are described in this report. Similarities and differences between this and other smoke constituent yield studies are discussed. This study provides contemporary data for commercial cigarettes available in the UK that are concordant with other studies. The major difference between the UK study and those in Australia, Canada or Massachusetts was the requirement to include cigarette brands differing in blend from the typical "UK Virginia style". Thus, "US Blended" and "Dark Air-Cured" cigarettes were included. From the outset, based on known and published differences in smoke chemistry between tobacco types (14,15), it was expected that the inclusion of different blend types in one study could weaken potential functional relationships between NFDPM or CO yield and the yield of other smoke constituents.

It is not possible to state the yield of a smoke constituent without measuring it and in doing so it becomes automatically dependent upon product and measurement variability. In general, ISO 5725 acknowledges that the "absolute" yield of a brand should be the average of the yield measurements from many laboratories, on many occasions, based on testing of different samples of the brand (16). Therefore, the use of one-point-in-time laboratory measurements to represent the absolute yields of minor smoke constituents for cigarette brands, as required in the current study, is a concern. The methods of analysis and variability within data generated in this study are discussed in detail in appropriate sections below.

METHODS

Cigarette samples

All of the manufacturers with brands used in the study (see Appendix, Table A1) were contacted during the period from September to November 2001 and each provided LGC with 2000 cigarettes from a single production batch, in retail outers of 10 s or 20 s. The cigarette packets for each brand were mixed and stored at 4 ˚C until required.

The manufacturers retained additional samples from the same batch of certain brands for further analysis.

Smoking parameters

Cigarettes were conditioned and smoked according to the parameters defined by the appropriate ISO standards (17,18), which were developed for NFDPM, nicotine and CO measurements. For measurement of some of the analytes included in the current study, it was necessary to introduce additional trapping devices that may have produced deviation from the parameters specified in ISO 3308. These are outlined as follows:

- The whole of the flow path between the cigarette and suction source should not exceed 300 Pa (Clause 4.1).
- The standard puff duration shall be 2.00 ± 0.02 s (Clause 4.2).
- The puff volume shall be 35 ± 0.3 mL with a series pressure drop of 1 kPa and > 95% should leave the butt in one standard puff duration (Clause 4.3).
- The puff profile shall be bell-shaped with a maximum flow rate of 25–30 mL/s between 0.8 and 1.2 s, and not more than 1 point of inflexion on the front and back edge (Clause 4.5).
- The total dead volume between the cigarette and suction source should not exceed 100 mL (Clause 5.3.5).

- The increase in pressure drop of the trap shall not exceed 250 Pa during the course of the measurement (Clause 5.4.7).
- The standard value of air velocity shall be 200 mm/s (Clause A.5)

The effect of using different smoke trapping methods for some smoke analytes needs to be assessed against these clauses and, for some methods, the conditions may be impossible to achieve. Nonetheless, despite these reservations, a 35-mL puff of 2 seconds duration taken once every 60 seconds were the primary target smoking parameters for all analytes.

Analytical techniques

With the exception of NFDPM, nicotine and CO, there are no internationally validated methods for smoke constituent analysis. LGC used in-house methods and performed a validation exercise or presented data from previous validation studies to demonstrate that each method was "fit for purpose" before commencing the benchmark study analysis. The validation exercise addressed several methodological criteria; i.e. under ideal conditions the method chosen should:

- Be capable of analysing 130 samples within a reasonable timeframe.
- Determine analyte yields with suitable precision between replicates.
- Distinguish between cigarette yields allowing ranking of brands.
- Be accurate and give good comparison with yields of 1R4F and 1R5F reference cigarettes as reported by other laboratories.
- Give relevant limits of detection and quantification to allow measurements at levels found in the chosen products.
- Show good analyte recovery.

Other criteria, such as reproducibility and repeatability in other laboratories, were beyond the scope of this study but were specified by LGC as desirable. In practice, LGC worked independently on the method development, seeking technical input from TMA Member Company scientists, and then formed a judgement concerning the adequacy of each method. After this, LGC performed a validation exercise with several cigarettes for which smoke constituent yields had already been published (18) and the Kentucky reference cigarettes, 1R4F and 1R5F, prior to commencing the "benchmark run".

The methods chosen are described in detail in the reports available on the internet (www.the-tma.org.uk) and are summarised and compared with those recommended by Health Canada and those used in the Massachusetts Benchmark Study in Table 1.

As evident from Table 1, with the exception of nitrosamines formed from nicotine and related alkaloids and often called the tobacco-specific nitrosamines (TSNA), all of the analytical methodologies employed in the present study closely follow those used in the other benchmark studies. The actual number of cigarettes used to achieve one result differed between methods, due primarily to constituent yield and the limit of detection (LOD) or limit of quantification (LOQ) for each method. The present study utilises liquid chromatography-mass spectrometry-mass spectrometry (LC-MS-MS) for the determination of TSNA. In contrast, other studies used gas chromatography with thermal energy analysis (GC-TEA). LC-MS-MS is a relatively new technique that rapidly has gained acceptance for the accurate determination of compounds in difficult matrices. It was not widely available at the time of the previous studies.

RESULTS AND ANALYSIS

Cigarette characteristics, yields and simple regression analysis

The characteristics of the cigarette brands used in this study are summarized in the Appendix, Table A1. We note that it is unusual to cover more than one cigarette blend style within a "benchmark study" but the UK Department of Health required that a wide range of product styles commercially available in the UK be tested and that all major manufacturers and importers be included. They also asked that the brands reflect a high percentage market share. The brands chosen accounted for approximately 58% of the UK market at the time of this request (July 2001).

The yields of all smoke constituents are summarised in the Appendix, Table A2. A mean yield for each smoke constituent by brand is shown along with the coefficient of variation (CoV). Groups of smoke constituents were assayed and reported together in 12 stand-alone reports. These reports and a Final Report are available online at www.the-tma.org.uk.

In this study, 4 analytes (arsenic, selenium, nickel and chromium) were either not detected or were below the limit of quantification for most of the cigarettes tested. Thus, they have been excluded from all of the results presented in this paper. Two other analytes (cadmium and lead) were detected in some but not all of the brands tested. Apart from these analytes, 10 others were detected with yields in the nanogram per cigarette range, 25 in the microgram per cigarette range and 3 (NFDPM, nicotine and CO) in the milligram per cigarette range.

An analysis of the replicate measurements for each brand-constituent combination, using both Cochran's test and Grubbs' test, identified no outliers. Thus all individual measurements were used in the calculation of the mean constituent yields shown in the Appendix, Table A2.

These mean smoke constituents yields were then used in simple regression models against NFDPM and CO yields. This is presented in Table 2 which shows the number of brands (from a total of 25) for which results were obtained, the mean smoke constituent yield and units of this value along with the CoV, the regression estimates following a least squares linear model and the R^2 value for the regressions.

Once a regression analysis was performed, outlying observations were identified using the studentised residual statistic (20). Only those brand-constituent combinations significant at the 99% level were regarded as "regression outliers". As an example, the outlying observation identified in the nitric oxide (NO) vs. NFDPM regression model is illustrated in Figure 1.

Table 1. Comparison of methods used in the UK study, with those recommended by Health Canada and those used in the Massachusetts benchmark study [a,b]

Analytes	Methods used in UK Study	Methods recommended by Health Canada (1999) and used subsequently in the Australian Study (2000)	Massachusetts benchmark exercise methods [c]
Carbonyls	linear smoker (2), LI, DNPH derivative, HPLC, DAD WS	linear smoker (10), LI, DNPH derivative, HPLC, UV	*PM*: linear smoker (3 cigs (TPM < 2 mg/cig), 1 cig (TPM >2 mg/cig), LI, DNPH derivative, HPLC
Nitric oxide	rotary smoker (1), GA, CL	single-channel smoker (1), GA, CL	*Lorillard*: single-channel smoker (1), GA, CL
Benzo[*a*]pyrene	linear smoker (5), CFP, GC-MS (SIM)	linear smoker (5), CFP, SPE, reverse phase HPLC fluorescence	*B&W*: linear smoker (10), CFP, SDE, GC-MS (SIM)
Ammonia	linear smoker (8), LI, IC	rotary smoker (10), CFP, LI, IC	*RJR*: rotary smoker (5), ET, CFP, LI, IC
Hydrogen cyanide	linear smoker (2), CFP/SG, chloramine-T UV/VIS spectrophotometer	linear smoker (5), CFP, LI , chloramine-T colorimetric CFA	*Lorillard*: linear smoker (1), CFP, LI, chloramine-T colorimetric CFA
Semi-volatile compounds	rotary smoker (5), CFP, XAD-4, GC-MS	linear smoker (20), CFP, CLI, GC-MS	*PM*: pyridine, quinoline rotary smoker (2), CFP, XAD-4, GC-MS
Nitrosamines	linear smoker (5), CFP, HPLC-MS-MS	linear smoker (10), CFP, column chromatography, GC-TEA	*B&W*: rotary smoker (10), ATCFP, SFE, GC-TEA
Volatile organic compounds	rotary smoker (5), CFP, CLI, GC-MS	linear smoker (10), CFP, CLI, GC-MS	*RJR*: styrene rotary smoker (10), CLI, GC-MS (SIM)
Phenols	linear smoker (5), CFP, HPLC fluorescence	linear smoker (5), CFP, reverse phase HPLC fluorescence	*Lorillard*: linear smoker (3), CFP, HPLC fluorescence
Metals	rotary smoker (20), ET, ICP-MS	rotary smoker (20), ET, microwave digestion, AAS or GFAAS	*PM*: rotary smoker (30 cigs (TPM 1–3 mg/cig), 20 cigs (TPM 4–9 mg/cig), 10 cigs (TPM ≥10 mg/cig), ET Cr: GFAAS, other metals: ICP MS
Mercury	rotary smoker (20), LI, CVAAS	rotary smoker (20), LI, microwave digestion, CVAAS	*PM*: rotary smoker (10), LI, microwave digestion, CVAAS
Aromatic amines	linear smoker (5), CFP, PFPA derivative, GC-MS (SIM)	Rotary smoker (10), CFP, PFPA derivative, GC-MS	*RJR*: linear smoker (1), CFP, SPE, PFPA derivative, GC-MS (SIM)

[A] Abbreviations: AAS = atomic absorption spectrometry, ATCFP = acid-treated Cambridge filter pad, CFA = continuous flow analysis, CFP = Cambridge filter pad, CL = chemiluminescence, CLI = one or more chilled liquid impinger, CV = cold vapour, DAD = diode array detector, DNPH = 2,4-dinitrophenylhydrazine, ET= electrostatic trap, GA = gas analysis, GC = gas chromatography, GF = graphite furnace, HPLC = high performance liquid chromatography, IC = ion chromatography, ICP = inductively-coupled plasma, LC = liquid chromatography, LI = one or more liquid impinger, TEA = thermal energy analyser, MS = mass spectroscopy, PFPA = pentafluoropropionic anhydride, SDE = steam distillation/extraction, SFE = supercritical fluid extraction, SG = silica gel, SIM = single ion monitoring, SPE = solid phase extraction, UV/VIS = ultraviolet/visible detection, WS = whole smoke, XAD-4 = an amberlite adsorbent resin.

[b] Figures in brackets give the number of cigarettes smoked per replicate.

[c] Company name in Massachusetts column indicates testing laboratory used.

Regression outliers are discussed in more detail below. Following the identification of the regression outliers, the relevant regression models were re-run excluding these observations. The R^2 values from these new regression analyses are presented in Table 2, adjacent to the original R^2 data.

All of the regression results shown in Table 2, except for *N*-nitrosonornicotine (NNN), were significant at $p < 0.05$ level before the exclusion of any outliers. The regression between NNN and NFDPM was significant at $p < 0.10$. For most of the volatile smoke constituents the regression fits were better for CO than for NFDPM.

A summary of the R^2 values and the level required to achieve statistical significance is presented in Figure 2. The figure is based on the R^2 value for each smoke constituent obtained from the regression analysis in Table 2 for both the CO and the NFDPM yield. Segregation into particulate phase or vapour phase for the predominant location of the constituent is denoted by filled or open symbols. The vertical axis records the cumulative frequency of the number of smoke constituent regressions with R^2 values equal to or lower than the stated value on the horizontal axis. Dashed lines are positioned to show the critical values that the R^2 must exceed to achieve significance at the 95% or the 99% level. This confirms, in a simple visual manner, the high significance levels obtained for the regression models.

In summary, the regression models of these smoke constituents showed statistically significant fits against NFDPM yield and for most volatile constituents the fit was improved by regressing against CO yield. Additionally, the exclusion of certain brand-analyte combinations, identified as regression outliers, also improved the fit of simple regressions against either NFDPM or CO yield.

Cigarette design features

Three different but complementary approaches were adopted to consider, within the limitations of the study, the

Table 2. Overall data and regression analysis summary [a]

Analyte	No. of brands	Units	Mean of all brands		Regression analysis of analyte yield vs. NFDPM				Regression analysis of analyte yield vs. CO			
			Analyte yield	CoV (%)	Slope	Intercept	R^2	R^2 w/o outliers	Slope	Intercept	R^2	R^2 w/o outliers
NFDPM	25	mg/cig	7.66	6.7	n/a	n/a			0.918	0.279	0.89	0.95
Nicotine	25	mg/cig	0.61	5.2	0.068	0.090	0.94	0.99	0.061	0.115	0.81	
CO	25	mg/cig	8.04	5.6	0.967	0.632	0.89	0.95	n/a	n/a		
Acetaldehyde	25	µg/cig	489.36	7.0	57.092	51.779	0.87		58.579	18.225	0.97	
Acetone	25	µg/cig	213.36	7.1	23.634	32.177	0.89		24.015	20.177	0.97	
Acrolein	25	µg/cig	42.09	9.4	5.335	1.198	0.84		5.433	−1.609	0.91	0.96
Butyraldehyde	25	µg/cig	29.54	9.4	3.456	3.058	0.89		3.433	1.932	0.92	
Crotonaldehyde	25	µg/cig	16.32	9.8	2.409	−2.135	0.90		2.338	−2.475	0.89	
Formaldehyde	25	µg/cig	22.27	14.9	3.486	−4.449	0.69		3.456	−5.528	0.72	
Methyl ethyl-ketone	25	µg/cig	56.78	7.7	6.811	4.585	0.90		6.847	1.719	0.96	
Propionaldehyde	25	µg/cig	35.64	7.9	4.110	4.138	0.88		4.164	2.152	0.96	
Nitric oxide	25	µg/cig	93.49	7.9	11.326	6.715	0.54	0.74	11.440	1.512	0.58	0.81
Benzo[*a*]pyrene	25	ng/cig	9.31	19.3	1.058	1.159	0.82		1.010	1.143	0.79	
Ammonia	25	µg/cig	4.32	23.9	0.599	−0.296	0.37	0.58	0.541	−0.056	0.32	0.45
HCN	25	µg/cig	83.96	11.1	11.503	−4.249	0.93		11.207	−6.224	0.93	
Pyridine	25	µg/cig	5.74	20.3	1.039	−2.207	0.68	0.90	0.932	−1.740	0.58	0.72
Quinoline	25	µg/cig	0.21	23.9	0.027	0.004	0.87		0.024	0.024	0.68	
Styrene (SVC)	25	µg/cig	5.03	17.0	0.718	−0.444	0.92		0.695	−0.533	0.91	
NAB	25	ng/cig	6.83	10.5	1.048	−1.215	0.22	0.59	0.979	−1.057	0.20	0.47
NAT	25	ng/cig	40.93	10.6	4.913	3.287	0.38	0.47	4.499	4.752	0.33	0.38
NNK	25	ng/cig	37.60	12.7	6.096	−9.144	0.21	0.52	5.905	−9.915	0.21	0.48
NNN	25	ng/cig	53.39	10.2	9.653	−20.589	0.14	0.28	9.032	−19.247	0.12	0.20
Acrylonitrile	25	µg/cig	6.79	9.6	0.938	−0.392	0.92		0.916	−0.572	0.93	
Benzene	25	µg/cig	34.21	7.2	3.726	5.659	0.87		3.798	3.671	0.95	
Isoprene	25	µg/cig	251.49	7.0	25.965	52.472	0.86		26.073	41.782	0.92	
Styrene (VOC)	25	µg/cig	5.66	12.8	0.924	−1.422	0.89		0.904	−1.609	0.90	
Toluene	25	µg/cig	57.21	7.8	7.056	3.115	0.90	0.95	7.075	0.295	0.96	
1,3-Butadiene	25	µg/cig	25.22	7.7	2.680	4.680	0.86	0.93	2.776	2.896	0.97	
Catechol	25	µg/cig	45.08	5.7	4.676	9.243	0.82		4.224	11.104	0.71	
Hydroquinone	25	µg/cig	39.52	6.3	4.208	7.270	0.82		3.854	8.529	0.72	
Phenol	25	µg/cig	12.74	11.8	2.013	−2.688	0.61	0.84	1.412	1.380	0.31	0.73
Resorcinol	25	µg/cig	0.88	6.1	0.104	0.084	0.85	0.94	0.097	0.098	0.79	
m- & *p*-Cresol	25	µg/cig	7.74	9.8	1.104	−0.716	0.73	0.86	0.850	0.908	0.46	0.76
o-Cresol	25	µg/cig	3.18	11.3	0.475	−0.456	0.68	0.84	0.354	0.335	0.40	0.75
Cadmium	24	ng/cig	17.66	11.9	3.035	−5.729	0.32	0.42	3.011	−6.705	0.33	0.43
Lead	22	ng/cig	11.36	16.0	1.868	−2.314	0.75		1.913	−3.429	0.80	
Mercury	25	ng/cig	1.70	10.1	0.166	0.428	0.72	0.85	0.168	0.347	0.78	0.89
Arsenic	3	ng/cig	insufficient res.									
Chromium	0	ng/cig	insufficient res.									
Nickel	0	ng/cig	insufficient res.									
Selenium	1	ng/cig	insufficient res.									
1-Naphthylamine	25	ng/cig	6.20	10.9	0.631	1.364	0.65	0.84	0.565	1.662	0.55	0.66
2-Naphthylamine	25	ng/cig	3.74	11.7	0.372	0.889	0.54	0.73	0.344	0.969	0.49	0.62
3-Aminobiphenyl	25	ng/cig	0.91	10.9	0.091	0.219	0.45	0.73	0.085	0.227	0.42	0.65
4-Aminobiphenyl	25	ng/cig	0.72	12.0	0.065	0.221	0.46	0.69	0.059	0.241	0.41	0.56

[a] Abbreviations: CO = carbon monoxide, HCN = hydrogen cyanide, insufficient res. = insufficient results (see text for details), n/a = not applicable, NAB = *N*-nitrosoanabasine, NAT = *N*-nitrosoanatabine, NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone, NNN = *N*-nitrosonornicotine, SVC = semi-volatile constituents (method), VOC = volatile organic constituents (method).

influence of cigarette design features on smoke constituent yields: 1) examination of outliers, 2) normalised constituent yields and 3) multiple regression analysis.

Examination of outliers: Regression outliers were identified using the studentised residual statistic and are displayed in Table 3. Note that the sign of the studentised residual statistic indicates whether the brand average is higher (+) or lower (–) than the other observations. An examination of the data in Table 3 shows that three distinct groups of outliers stand out:

1) nitrogen-containing smoke constituents for the brand Gitanes Caporal Filter;
2) volatile or gaseous constituents for the brand Senior Service; and
3) alkyl phenols for the brand Senior Service.

Remaining outliers were trace metals and very low-yield constituents. This may reflect real experimental error

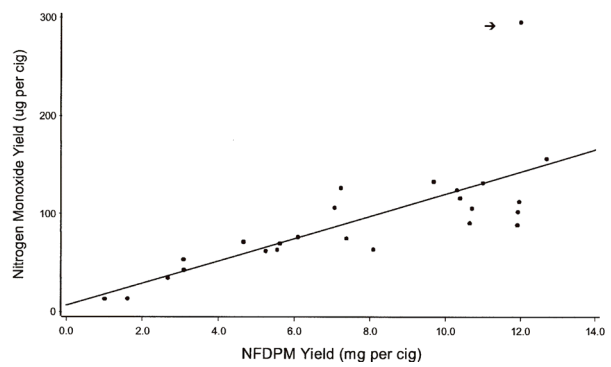

Figure 1. Regression of NO yield vs. NFDPM yield. Each brand's NO yield and NFDPM yield is shown as a single point. The one brand identified as a regression outlier using the studentised residual statistic ($p < 0.01$) is marked with an arrow.

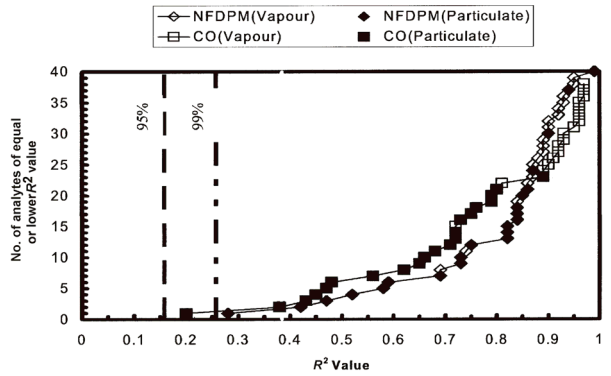

Figure 2. Cumulative distribution of R^2 values (outliers removed) for analyte yield correlations with NFDPM and CO yield

resulting from the use of non-standardised and perhaps non-robust methods, especially those near their LOD.

From an examination of the brand attributes (Appendix, Table A1), it is apparent that Gitanes Caporal Filter is the only dark air-cured blend style cigarette included in this study and Senior Service is the only unfiltered ("plain") cigarette in this study. Dark air-cured tobaccos are known to have a high nitrogen content (21) and it is unsurprising that yields of nitrogen-containing smoke constituents are greater for this brand. Two known features may account for the outlying results obtained with the brand Senior Service. First, the paper porosity of Senior Service is the highest in the study (200 CU) and increased paper porosity is associated with lower relative yields of gaseous constituents in mainstream smoke (22,23). Second, cellulose acetate filters are known to selectively trap alkyl phenols in smoke (24), and because Senior Service is unfiltered, it should have relatively higher yields of these compounds.

Normalised constituent yields: The study was not designed to permit a complete investigation of the potential impact of cigarette design features on the variation of smoke constituent yields. By seeking to capture all of the cigarette design features available in a "market survey" approach, an in-depth analysis of the impact of any one feature on smoke constituent yields could not be discerned because each variable was not altered in an independent, systematic and controlled manner. However, it was felt that the impact of cigarette design features on smoke constituent yield variability might be seen by extending the regression

Table 3. Regression outliers

Parameter	Brand	Studentized residual	Probability level
	NFDPM outliers		
Carbon monoxide	Senior Service	−5.46	0.0013
Nicotine	Gitanes Caporal	−8.84	<.0001
Nitric oxide	Gitanes Caporal	+8.16	<.0001
Ammonia	Gitanes Caporal	+9.50	<.0001
Pyridine	Gitanes Caporal	+10.75	<.0001
NAB	Gitanes Caporal	+20.11	<.0001
NAT	Gitanes Caporal	+6.35	0.0003
NNK	Gitanes Caporal	+17.86	<.0001
NNN	Gitanes Caporal	+20.19	<.0001
Toluene	Senior Service	−4.57	0.0053
1,3-Butadiene	Senior Service	−4.91	0.0031
Phenol	Senior Service	+9.87	<.0001
Resorcinol	Gitanes Caporal	−5.57	0.001
o- & p-Cresol	Senior Service	+6.60	0.0002
o-Cresol	Senior Service	+7.87	<.0001
Lead	Superkings	−4.76	0.0039
Cadmium	Gitanes Caporal	+7.57	<.0001
Mercury	Red Band Lights	+4.46	0.0063
1-Naphthylamine	Gitanes Caporal	+8.35	<.0001
2-Naphthylamine	Gitanes Caporal	+7.67	<.0001
3-Aminobiphenyl	Gitanes Caporal	+11.01	<.0001
4-Aminobiphenyl	Gitanes Caporal	+9.15	<.0001
	CO outliers		
NFDPM	Senior Service	+5.74	0.0008
Acrolein	Gitanes Caporal	−4.82	0.0036
Nitric oxide	Gitanes Caporal	+9.24	<.0001
Ammonia	Gitanes Caporal	+8.38	<.0001
Pyridine	Gitanes Caporal	+6.59	0.0002
NAB	Gitanes Caporal	+17.78	<.0001
NAT	Gitanes Caporal	+5.96	0.0005
NNK	Gitanes Caporal	+17.21	<.0001
NNN	Gitanes Caporal	+19.17	<.0001
Phenol	Senior Service	+9.92	<.0001
m- & p-Cresol	Senior Service	+7.66	<.0001
o-Cresol	Senior Service	+8.74	<.0001
Cadmium	Gitanes Caporal	+7.60	<.0001
Mercury	Red Band Lights	+4.98	0.0028
1-Naphthylamine	Gitanes Caporal	+5.95	0.0006
2-Naphthylamine	Gitanes Caporal	+6.62	0.0002
3-Aminobiphenyl	Gitanes Caporal	+9.68	<.0001
4-Aminobiphenyl	Gitanes Caporal	+7.84	<.0001

analysis presented above. In this extension, all of the smoke constituent yields were normalised and used in a further regression model against NFDPM yield, as follows. For each smoke constituent the average yield across all brands was calculated and the individual brand constituent yields were then expressed as a percentage of this average. These values for all smoke constituents and all brands were used in a regression analysis against each brand's measured NFDPM yield (Figure 3). Each point on Figure 3 represents a yield for a single constituent from a single brand. Regression outliers from the individual constituent yield models have been excluded. Thus, there are 978 data points on this figure and, for clarity, all normalised constituent yields from a single blend style are shown with the same symbol. This approach permits constituents with a wide difference in yields (i.e. those in the few nanogram range such as benzo[*a*]pyrene (B[*a*]P) to those in the hundreds of microgram range such as acetaldehyde to be compared on the one

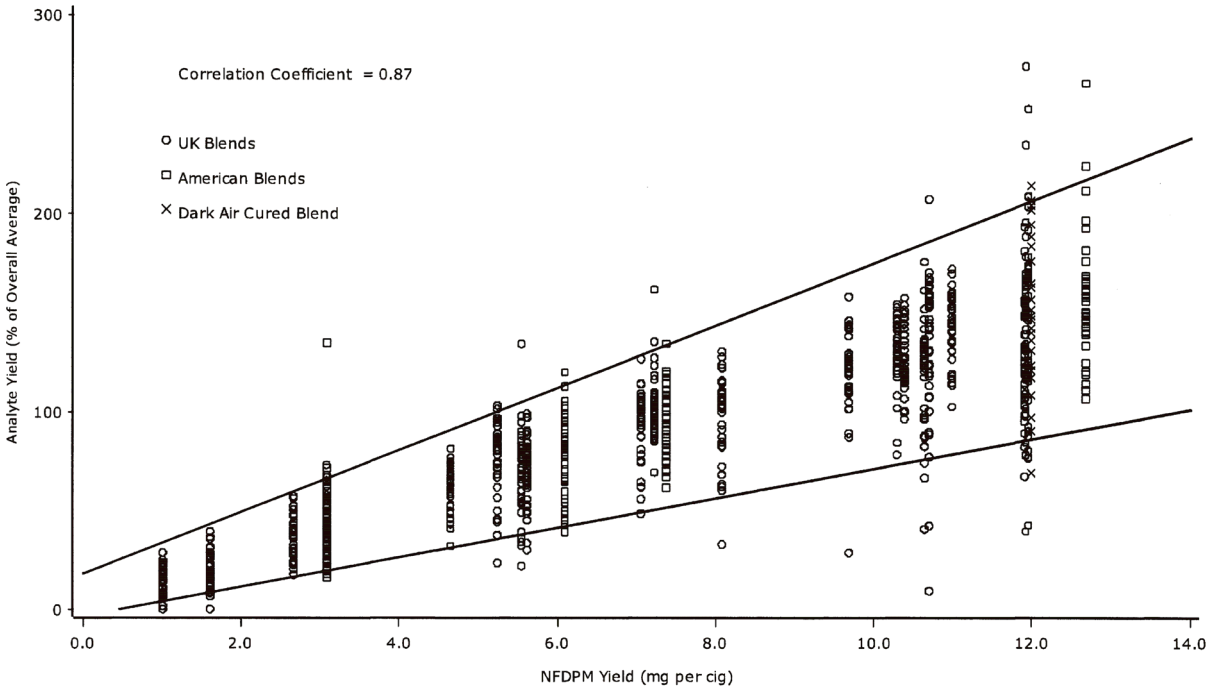

Figure 3. Smoke constituent yields expressed as a percentage of the mean yield per constituent. For each smoke constituent the average yield across all brands was calculated and the individual brand constituent yields were then expressed as a percentage of this average. These values were used in a regression analysis against each brand's measured NFDPM yield. Regression outliers from the individual constituent's yield vs. NFDPM yield models have been excluded.

graph. Clearly, there are limits to this approach but the overall conformity to a common least squares regression line ($r = 0.87$, $R^2 = 0.76$) suggests a strong and highly significant correlation between all smoke constituent yields and a brand's NFDPM yield. The high R^2 is remarkable because the great majority of smoke constituents (97.8%) from all of the blend styles in the study are included in this correlation. Within the limits of this approach, this suggests that the brand's NFDPM yield can give a reliable indication of the yield of the other smoke constituents.

Multiple regression analysis: To provide a more complete quantitative assessment of the design feature effects on constituent yield, a multiple regression approach was adopted. If the contribution of a design feature parameter to the variation in the smoke constituent yields were significant, then its addition to the NFDPM regression models would result in a significantly improved R^2.

Prior to the multiple regression analysis, the correlation matrix between the design feature parameters and NFDPM yield was derived. These correlations are shown in Table 4, together with the *p*-values relevant to the hypothesis that the observed correlation is zero.

From this table several obvious significant correlations are apparent: the presence or absence of a filter is highly correlated with paper porosity; length is highly correlated with circumference; weight is highly correlated with NFDPM, filter ventilation, paper porosity, and circumference; filter ventilation is highly correlated with NFDPM. Such high correlations are not surprising because this study was not specifically structured to separate the known covariance of design parameters and their effect on smoke constituent yields.

In a regression context, high correlations between independent variables will result in unstable effect estimates with high standard errors. Given the high correlation between NFDPM yield and the level of filter ventilation, the effect of filter ventilation, independent of the direct effect upon NFDPM yield, cannot be estimated. Similarly, the effect of paper porosity cannot be separated from the effect of plain vs. filtered cigarette. Therefore, only one parameter each from these two pairs of correlations was included in the multiple regression models. Based on an examination of the data, the remaining high correlations were not expected to have a noticeable adverse effect upon the multiple regression models. Thus, the following set of design parameters were included in the regression models between constituent yield and NFDPM yield:

- Blend Style [UK (1), American (2), Dark (3)]
- Menthol (presence or absence)
- Paper Porosity
- Circumference
- Weight
- Length

By use of the stepwise selection method (25), an improvement in R^2 values following the addition of each of the design feature parameters was noted (illustrative examples are shown in Table A3 which is appended). The reported significance level for each parameter, adjusted for all effects in the total model, was used to assess whether that parameter made a significant contribution to the variation observed in the smoke constituent yields. This multiple regression analysis revealed the following:

- The presence or absence of menthol in a brand, the cigarette length and the cigarette weight had no statistically significant effect upon the yield of any of the 40 smoke constituents.
- Cigarette circumference had a significant effect for 9 of the 40 smoke constituents; however the change in R^2 was negligible.

Table 4. Multiple regression analysis correlation matrix

Parameters	NFDPM	Blend style	Filter	Menthol	Filter vent	Paper porosity	Circumference	Weight	Length
NFDPM	1	0.16	−0.24	−0.15	**−0.95**	0.14	0.01	**0.53**	−0.06
	—	*0.4495*	*0.2437*	*0.4786*	***<.0001***	*0.5188*	*0.9657*	***0.0065***	*0.781*
Blend style	0.16	1	0.10	−0.14	−0.01	**−0.34**	−0.08	−0.07	−0.22
	0.4495	—	*0.6493*	*0.5102*	*0.9568*	***0.0967***	*0.6905*	*0.7378*	*0.2967*
Filter	−0.24	0.10	1	0.06	0.28	**−0.88**	−0.08	−0.27	**0.34**
	0.2437	*0.6493*	—	*0.7750*	*0.1722*	***<.0001***	*0.7043*	*0.1894*	***0.095***
Menthol	−0.15	−0.14	0.06	1	0.17	−0.08	0.06	−0.09	−0.08
	0.4786	*0.5102*	*0.7750*	—	*0.4257*	*0.7205*	*0.7674*	*0.6840*	*0.7158*
Filter ventilation	−0.95	−0.01	0.28	0.17	1	−0.20	−0.07	**−0.49**	0.07
	<.0001	*0.9568*	*0.1722*	*0.4257*	—	*0.3494*	*0.7331*	***0.0139***	*0.7411*
Paper porosity	0.14	**−0.34**	**−0.88**	−0.08	−0.20	1	0.14	**0.44**	−0.09
	0.5188	***0.0967***	***<.0001***	*0.7205*	*0.3494*	—	*0.5116*	***0.0297***	*0.6843*
Circumference	0.01	−0.08	−0.08	0.06	−0.07	0.14	1	**0.49**	**−0.51**
	0.9657	*0.6905*	*0.7043*	*0.7674*	*0.7331*	*0.5116*	—	***0.0130***	***0.0084***
Weight	0.53	−0.07	−0.27	−0.09	**−0.49**	**0.44**	**0.49**	1	0.11
	0.0065	*0.7378*	*0.1894*	*0.6840*	***0.0139***	***0.0297***	***0.0130***	—	*0.593*
Length	−0.06	−0.22	**0.34**	−0.08	0.07	−0.09	**−0.51**	0.11	1
	0.7810	*0.2967*	***0.0950***	*0.7158*	*0.7411*	*0.6843*	***0.0084***	*0.5930*	—

Arabic numerals are the correlation coefficients for the appropriate pair, with the associated *p*-value shown in italics beneath. Values that are statistically significant ($p < 0.05$) are shown in bold type.

- The effect of paper porosity (or equally, presence or absence of a filter) was significant for 11 of the 40 constituents: the most noticeable improvements in R^2 values were for the alkyl phenol compounds.
- Blend style was significant for 26 smoke constituents; although, for many, the effect on R^2 was small. The most noticeable increases in R^2 were observed for the nitrogen-containing constituents.

Thus, based on multiple regression analysis within this study, the only design features to have large and statistically significant effects upon smoke constituent yields were cigarette blend style and plain vs. filtered cigarettes.

Analytical considerations

The analysis of a large number of smoke constituents from any cigarette is not a trivial exercise. Sources of variability that may be encountered in the analysis of a product made from natural materials include: 1) the product itself; 2) laboratory analytical procedures, i.e. methodological errors; and 3) repeat analysis errors. It should be noted that the last source includes only short-term variability for this study but would also include long-term and inter-laboratory variability for measurements over extended timescales in more than one laboratory. Each of these possible sources of variability is addressed below by considering the present study and, where appropriate, comparing the findings with those from other studies.

Product variability: For any product made from natural materials grown in different world regions, batch variability and seasonal variation should be expected. Thus, identical yields would not necessarily be expected from a different sample of the same brand of cigarettes, especially for smoke constituents that may be present in very low concentrations.

ISO 8243 (26) recognises the need to test samples taken over a period of time to allow for product variability in the measured yield. In the UK, for example, routine surveys of NFDPM, nicotine and CO yields involve testing matched samples of cigarettes at both LGC and the manufacturing company's laboratories at 2-month intervals. The test samples are drawn from samples taken at 2-week intervals throughout each sampling/test period.

In the present study, the protocol required the manufacturers to sample a single batch of each cigarette brand. Therefore, the smoke constituent analyses would not include the increased variability associated with the natural product changes over production runs and over a period of time. There is no way of knowing how closely the measured yields reflect the average yields of the specified brands. At best, results from this one-point-in-time study should only be used to rank products at the time of sampling and cannot be used as absolute measures of yields. It is also possible that the relative ranking may change for repeated yield measurements on different samples.

Within laboratory analytical variability: Numerous factors may affect the variability encountered in analysing the yield of a smoke constituent. In establishing methods of analysis, several sources of variability need to be taken into account. Because of the complex task of analysing 44 analytes in cigarette smoke, many sources of variability can be an issue. Table A4 (appended) identifies these possible sources and suggests examples when they might have affected the analytical results. During the study, steps were taken to minimise the impact of such variability on the quality of data emerging from each method; however, it is impossible to establish how successful these steps were.

Although the list in Table A4 is not exhaustive, it highlights the difficulties involved in establishing the methods for smoke constituent analysis. One source of variability

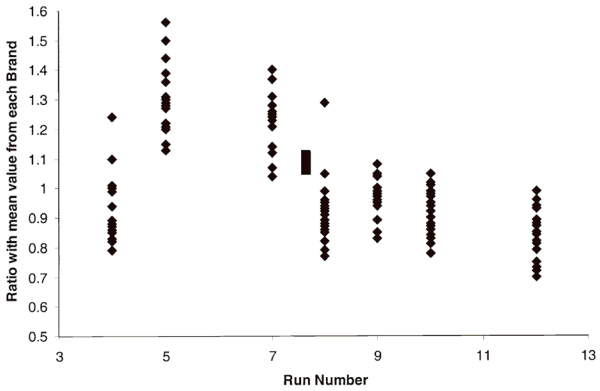

Figure 4. Variability between smoking machine runs for benzo[*a*]pyrene

Table 5. Analysis of variance between brands and runs

Constituent	CoV	Percentage of variation		
		Between brands	Between runs	Residual
CO	6.7	80.5	0.3	19.2
NFDPM	5.6	83.6	0.3	16.2
Formaldehyde	14.9	75.4	2.1	22.5
B[*a*]P	19.3	75.0	10.5	14.5
Ammonia	23.9	92.1	2.4	5.5
HCN	11.1	79.8	0.9	19.3

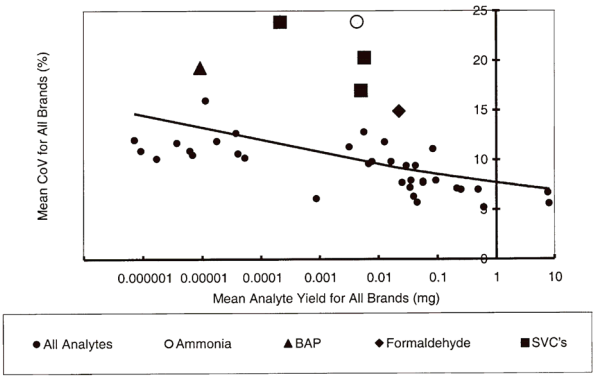

Figure 5. Variability in assays over a wide range of smoke constituent yields

that should be expected is the variability between smoking runs. In practice, therefore, replicates are spread randomly over a number of smoking runs to average run-to-run effects on yields for individual products.

As an example of this effect, the B[*a*]P yield variability between runs is illustrated in Figure 4, in which the individual replicate yield values for each brand were expressed as a ratio of the relevant brand average yield and plotted against run number. This permits the run-to-run variability to be visualised without being masked by the differences in yields between brands.

The CoVs shown for each analyte in Table 2 reflect the observed variability within this study and include run-to-run variability. The run-to-run component has been investigated for several analytes, by performing an analysis of variance. The proportions of the components attributable to brands, to runs and the residual (or unexplained component) for these analytes are shown in Table 5. Both the CoVs and between runs components are smallest for NFDPM and CO, the only constituents for which there are standard ISO methods of analysis.

Variability within the current data set: From the data presented in Table 2, a range of CoV values from 5.2% (for nicotine) to 23.9% (for ammonia and quinoline) was recorded. The general trend of increased CoV, as analyte yield decreased was apparent and is shown in Figure 5.

This higher CoV for lower yield constituents is consistent with findings in other areas of chemical analysis (27) and this provides some insight into the likely variability to be expected as standard methods for the analysis of smoke constituents are developed. Other features from the current study suggest that increased variability will be encountered if the use of smoke constituents analyses becomes widespread. For example, within the current study, although not in the original protocol, one smoke constituent (styrene) was analysed by two independent methods. A summary comparison of these two analyses for all cigarette brands and the reference cigarettes 1R4F and 1R5F is shown in Figure 6. These data are presented as a ratio of yields between the two methods: a volatile organic compound method (labelled VOC in the figure) or a semi-volatile constituent method (labelled SVC in the figure).

An equal yield in both assays would be reported as a ratio of 1.0. Across the 27 cigarette brands the yield ratios range from 0.75 to 2.4. Unsurprisingly, several brands showed a great difference in yield across the two analytical methods, emphasising the need for caution in attempting to compare smoke constituent yields across different methods of analysis.

Within-laboratory variability over an extended period of time: Labstat recently published smoke constituent yield data (28) on the 1R4F reference cigarette collected over an 11-month period. This was the first time that such long-term data had been published. The reported CoV range was 4.3% for NFDPM to 77.8% for selenium, based on 53–174 observations per analyte; 25 of the 44 constituents had a CoV of less than 10%. However, these CoV values do not describe the extremes of the range of yields that were obtained during this period of time. An estimate of the range of yields from that study can be obtained by comparing the original authors' highest likely values (obtained from the mean value +2 sd) with lowest likely values (mean −2 sd) for each analyte. After excluding the trace metals, this approach showed on average a 50% difference in yields between the likely highest and lowest reported values across all analytes: formaldehyde varied by over 200%. This analysis shows that long-term, within-laboratory variability may present considerable technical challenges in the measurement of these smoke constituent yields. The impact of such variability on measurement uncertainty and tolerances is discussed below.

Inter-laboratory variability: Another recent study (19) reported smoke constituent yields from a 'one-point-in-time' sample of three brands that were analysed in seven laboratories for as many of the 44 smoke constituents as the laboratories could measure at that time. Each laboratory used their preferred and internally validated methods. The study reported that no analytes had lower within-laboratory measurement variability than NFDPM, nicotine and CO, and

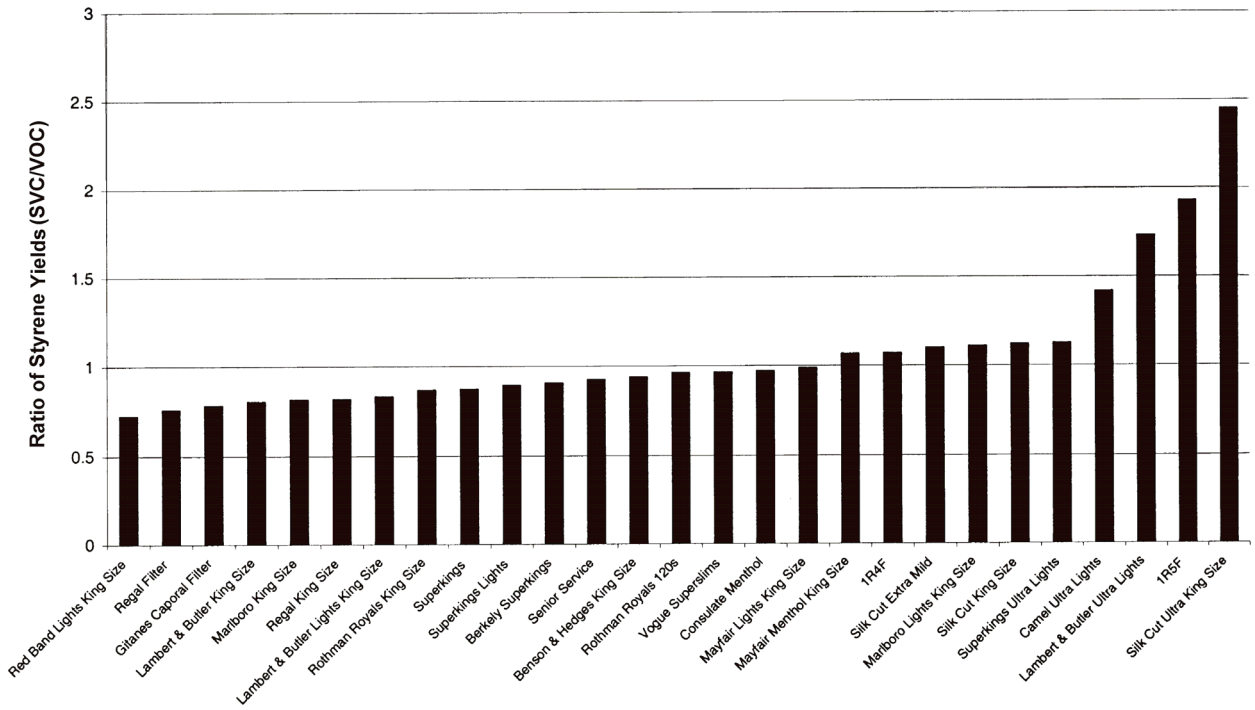

Figure 6. Comparison of styrene yields by two methods of analysis

70% of the other analytes had statistically-significantly higher levels of variability. The difference between the highest and lowest reported yield measurements, averaged for all constituents, was 80%, even when three analytes (mercury, styrene and resorcinol – for which reported yields gave in excess of an 8-fold range) were excluded. Analytes with the largest variability in reported yield between laboratories were mercury, resorcinol, styrene, quinoline, butadiene and ammonia.

The published study (19) suggests that the yields obtained by LGC in the current study may be quite different from those that might be obtained from other laboratories. This possibility was investigated by testing a subset of brands from the current UK study at an additional contract laboratory (Labstat), using samples from the same production batch. Five products from this manufacturing run of cigarettes (Regal KS, Superkings Lights, Silk Cut KS, Silk Cut Ultra KS, Rothmans Royals) along with the 1R4F reference cigarette were re-tested. Product samples were sent in December 2001 and smoke constituent yields data were reported in February 2002. The results are summarised in Table 6.

A similar level of variability between replicates was found in both contract laboratories (Labstat and LGC) and differences of less than 10% between the NFDPM, nicotine and CO yields were reported from the two laboratories, when averaged across all brands tested. However, some relatively large differences in absolute yields were reported between the two laboratories. This was highlighted by calculating ratios of the mean constituent yields per brand, which are shown in Table 6. From these data, ratios of 0.40 to 1.98 for individual smoke constituent yields were observed between the same brands across laboratories. From this comparison, constituents with the largest mean yield differences across the six cigarettes were ammonia, the four aromatic amines, crotonaldehyde and pyridine. It should be noted that the constituents in this group are different from the constituents reported to be most variable in the larger inter-laboratory study, discussed above (19).

Measurement uncertainty and tolerances: Within the 44 constituents examined in this study, three (CO, nicotine and NFDPM) are present in smoke in milligram quantities. Several others were either below the LOD or only found in nanogram amounts. They were arsenic, chromium, selenium, lead, mercury, nickel, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), *N*-nitrosoanatabine (NAT), *N*-nitrosoanabasine (NAB), NNN, B[*a*]P, 1-naphthylamine (1-NA), 2-naphthylamine (2-NA), 3-aminobiphenyl and 4-aminobiphenyl.

For the analysis of NFDPM and nicotine, ISO standards specify rigorous sampling procedures, smoking conditions and frequency of analysis (17,18,26). Despite this, and years of practical experience with these analyses, measurement tolerances of ± 15% with a minimum of ± 1 mg for NFDPM or 0.1 mg for nicotine, are required (26). Within the ISO standards, these tolerance values are increased further for single point in time samples. Furthermore, consistent with a recent review of available data (29), ISO 8243 has recently incorporated a 20% tolerance value for CO yield measurement. The ISO Working Group (ISO/TC126/WG8) is also reviewing the tolerances around NFDPM and nicotine yields. In the current study, all measured NFDPM yields fell within the existing tolerance values set by ISO 8423. The yields ranged from −13% to +12% around the declared yields except for one brand (L&B Ultra Lights) for which the yield was within the permitted 1 mg tolerance value.

For other smoke constituents much less data are available and the effects of product and measurement variability on

Table 6. Smoke constituent yields for five brands plus 1R4F tested in two laboratories

	1R4F			Regal KS			Superkings Lights			Silk Cut KS			Silk Cut Ultra KS			Rothmans Royals		
Analyte	LGC	Labstat	Ratio LGC/ Labstat	LGC	Labstat	Ratio LGC/ Labstat	LGC	Labstat	Ratio LGC/ Labstat	LGC	Labstat	Ratio LGC/ Labstat	LGC	Labstat	Ratio LGC/ Labstat	LGC	Labstat	Ratio LGC/ Labstat
NFDPM (mg/cig)	9.06	9.11	**0.99**	11.96	12.20	**0.98**	8.09	8.34	**0.97**	5.62	5.41	**1.04**	1.01	0.85	**1.19**	11.00	11.20	**0.98**
Nicotine (mg/cig)	0.71	0.75	**0.95**	0.90	0.97	**0.93**	0.70	0.76	**0.92**	0.50	0.52	**0.96**	0.11	0.10	**1.09**	0.89	0.98	**0.91**
CO (mg/cig)	12.26	11.40	**1.08**	13.86	13.70	**1.01**	7.54	7.28	**1.04**	5.78	5.17	**1.12**	1.20	0.96	**1.26**	10.86	10.80	**1.01**
Formaldehyde (µg/cig)	18.30	22.70	**0.81**	56.30	74.20	**0.76**	22.30	28.00	**0.80**	10.10	10.60	**0.95**		2.45		36.60	52.50	**0.70**
Acetaldehyde (µg/cig)	709.00	501.00	**1.42**	872.00	658.00	**1.33**	505.00	349.00	**1.45**	367.00	216.00	**1.70**	73.00	50.60	**1.44**	661.00	501.00	**1.32**
Acetone (µg/cig)	299.00	239.00	**1.25**	360.00	303.00	**1.19**	218.00	169.00	**1.29**	171.00	112.00	**1.53**	39.10	28.00	**1.40**	289.00	240.00	**1.20**
Acrolein (µg/cig)	55.00	47.30	**1.16**	87.80	83.80	**1.05**	43.40	37.40	**1.16**	28.70	21.30	**1.35**	4.30	4.67	**0.92**	62.40	58.30	**1.07**
Propionaldehyde (µg/cig)	52.80	44.30	**1.19**	62.10	55.20	**1.13**	37.60	30.60	**1.23**	27.10	18.80	**1.44**	5.70	4.91	**1.16**	48.60	43.30	**1.12**
Crotonaldehyde (µg/cig)	16.80	11.00	**1.53**	33.30	21.90	**1.52**	14.90	9.63	**1.55**	10.50	5.30	**1.98**				25.80	16.90	**1.53**
Methyl ethyl-ketone (µg/cig)	76.50	67.30	**1.14**	98.50	85.30	**1.15**	58.00	47.90	**1.21**	44.70	31.60	**1.41**	8.20	9.62	**0.85**	76.90	68.40	**1.12**
Butyraldehyde (µg/cig]	40.30	29.90	**1.35**	51.20	36.50	**1.40**	31.50	21.70	**1.45**	23.10	14.50	**1.59**	5.50	5.30	**1.04**	42.50	30.40	**1.40**
B[*a*]P (ng/cig)	7.07	6.42	**1.10**	15.61	13.20	**1.18**	12.10	8.28	**1.46**	6.85	6.05	**1.13**	1.68	1.24	**1.35**	15.97	13.40	**1.19**
Hydroquinone (µg/cig)	34.20	36.70	**0.93**	62.70	65.10	**0.96**	48.50	44.80	**1.08**	32.30	32.50	**0.99**	8.46	7.57	**1.12**	61.80	62.80	**0.98**
Resorcinol (µg/cig)	0.64			1.46	1.14	**1.28**	1.02	0.61	**1.66**	0.59						1.41	1.22	**1.16**
Catechol (µg/cig)	38.00	36.90	**1.03**	67.60	66.50	**1.02**	57.60	47.30	**1.22**	37.30	35.50	**1.05**	10.10	8.06	**1.25**	70.70	68.40	**1.03**
Phenol (µg/cig)	7.54	10.00	**0.75**	15.00	16.20	**0.93**	14.10	11.00	**1.28**	11.30	11.80	**0.96**	0.91			21.60	23.80	**0.91**
m- & p-Cresol (µg/cig)	5.88	7.61	**0.77**	9.08	10.90	**0.83**	8.94	7.60	**1.18**	6.97	7.51	**0.93**	0.80	0.80	**1.00**	11.70	13.80	**0.85**
o-Cresol (µg/cig)	3.31	2.98	**1.11**	3.69	4.19	**0.88**	3.68	2.85	**1.29**	2.89	3.01	**0.96**		0.29		4.84	5.59	**0.87**
1-Naphthylamine (ng/cig)	8.74	16.00	**0.55**	6.58	13.50	**0.49**	7.70			6.06	10.50	**0.58**	1.34	2.13	**0.63**	8.13	15.00	**0.54**
2-Naphthylamine (ng/cig)	6.71	10.70	**0.63**	3.38	8.45	**0.40**	4.58	8.47	**0.54**	3.16	6.70	**0.47**	0.86	1.41	**0.61**	5.05	9.08	**0.56**
3-Aminobiphenyl (ng/cig)	1.66	2.77	**0.60**	0.84	2.08	**0.40**	0.97	1.89	**0.51**	0.89	1.50	**0.59**	0.22	0.35	**0.63**	1.08	2.29	**0.47**
4-Aminobiphenyl (ng/cig)	1.30	2.22	**0.59**	0.63	1.58	**0.40**	0.78	1.56	**0.50**	0.71	1.27	**0.56**	0.21	0.29	**0.72**	0.81	1.79	**0.45**
NO (µg/cig)	276.00	283.00	**0.98**	113.00	129.00	**0.88**	64.10	69.70	**0.92**	70.30	76.30	**0.92**	13.70	15.50	**0.88**	116.00	164.00	**0.71**
HCN (µg/cig)	123.00	105.00	**1.17**	137.00	117.00	**1.17**	68.80	54.50	**1.26**	52.00	40.90	**1.27**	8.40	4.35	**1.93**	132.90	117.00	**1.14**
Ammonia (µg/cig)	6.20	11.20	**0.55**	5.40	9.74	**0.55**	3.60	6.69	**0.54**	2.60	5.36	**0.49**				5.00	10.80	**0.46**
1,3-Butadiene (µg/cig)	31.00	41.30	**0.75**	42.20	56.20	**0.75**	27.10	34.60	**0.78**	17.50	21.90	**0.80**	4.66	6.23	**0.75**	35.50	43.00	**0.83**
Isoprene (µg/cig)	343.00	377.00	**0.91**	369.00	369.00	**1.00**	266.00	253.00	**1.05**	190.00	178.00	**1.07**	50.30	57.60	**0.87**	361.00	346.00	**1.04**
Acrylonitrile (µg/cig)	8.07	10.10	**0.80**	11.70	12.60	**0.93**	6.93	6.62	**1.05**	4.38	4.30	**1.02**	0.76			9.61	10.70	**0.90**
Benzene (µg/cig)	40.60	38.50	**1.05**	57.50	51.00	**1.13**	37.60	30.80	**1.22**	26.30	21.90	**1.20**	6.25	6.10	**1.02**	48.00	40.60	**1.18**
Toluene (µg/cig)	72.30	67.10	**1.08**	97.70	79.80	**1.22**	59.20	45.70	**1.30**	41.20	32.20	**1.28**	7.56			82.80	65.50	**1.26**
Pyridine (µg/cig)	4.14	6.77	**0.61**	9.54	12.10	**0.79**	3.94	5.87	**0.67**	2.86	4.48	**0.64**	0.82	1.26	**0.65**	8.37	11.10	**0.75**
Quinoline (µg/cig)	0.22	0.25	**0.88**	0.27	0.34	**0.78**	0.22	0.19	**1.13**	0.16	0.20	**0.82**				0.34	0.41	**0.82**
Styrene (µg/cig)	5.63	7.21	**0.78**	9.70	9.10	**1.07**	4.42	4.44	**1.00**	3.31	3.72	**0.89**	0.93	1.82	**0.51**	7.70	8.42	**0.91**
NNN (ng/cig)	107.00	115.00	**0.93**	22.80	19.90	**1.15**	17.60	16.20	**1.09**	17.90	15.70	**1.14**	7.90	6.32	**1.25**	67.70	50.00	**1.35**
NAT (ng/cig)	113.00	129.00	**0.88**	31.50	38.00	**0.83**	29.70	28.70	**1.03**	27.60	28.70	**0.96**	10.20	7.78	**1.31**	47.00	44.70	**1.05**
NAB (ng/cig)	16.10	27.50	**0.59**	5.20	5.46	**0.95**	4.30	6.48	**0.66**	3.80	3.89	**0.98**	1.50	2.23	**0.67**	7.00	4.89	**1.43**
NNK (ng/cig)	93.00	90.80	**1.02**	30.20	26.80	**1.13**	23.40	22.40	**1.04**	19.80	18.60	**1.06**	6.50			49.20	37.70	**1.31**
Mercury (ng/cig)	4.30	4.83	**0.89**	2.20	3.03	**0.73**	1.40	2.08	**0.67**	1.40	2.25	**0.62**	0.30			2.00	3.03	**0.66**
Cadmium (ng/cig)	62.80	63.60	**0.99**	21.90	28.50	**0.77**	10.70	15.60	**0.69**	5.30	8.31	**0.64**				24.10	29.10	**0.83**
Lead (ng/cig)	41.40	37.10	**1.12**	19.30	21.60	**0.89**	12.10	14.80	**0.82**	5.50						17.40	20.10	**0.87**
Nickel (ng/cig)																		
Arsenic (ng/cig)	6.50	5.79	**1.12**															
Selenium (ng/cig)	<2.3																	

their absolute yields remain unknown. Although work on standardisation of some of these methods is progressing (30), it must be remembered that many of the smoke constituents are present in very low concentrations (parts per million of the particulate or gaseous phase of smoke). From the work described above, the following observations question the likelihood of achieving robust methods: the range of CoV values for smoke constituents in this study which typically were higher for lower yield constituents; the outcome of a direct comparison of smoke constituent yields between methods of analysis; the between laboratories comparison of a subset of brands; and the long-term variability within laboratory data. Thus, at the current state of smoke constituent analytical capability, it is highly likely that tolerance values to be associated with smoke constituent measurements, following method standardisation and inter-laboratory studies, would need to be greater than those for NFDPM, nicotine or CO measurement and in some cases, much greater.

Comparison with other benchmark studies

Results from several recent studies on the yields of 44 smoke constituents in cigarette brands are now available. Canadian benchmark studies have not yet been formally published, although data are available from the British Columbia website (31) that includes numerous Canadian brands analysed in 1999–2000. Only data on Canadian brands reported in 2000 were used in the comparisons below. Another 15-brand study of Australian cigarettes has been placed on the website of the Australian Federal Department of Health (13). The 1999 Massachusetts benchmark study on 26 brands is also available for comparison (11).

Within this group of studies, the Canadian and Australian studies generated data sets under ISO puffing regimes (as well as an "intense" smoking regime) but the Massachusetts study reported smoke constituent yield data only under the Massachusetts smoking regime (45-mL puff, 2 seconds duration, every 30 seconds with 50% of the filter ventilation taped over). Thus, Australian and Canadian data obtained at Labstat under the ISO smoking regime are more readily comparable with the current study. For this comparison, data obtained under the Canadian "intense" smoking regime are not included.

Correlations with NFDPM and CO across studies: R^2 values from linear regressions for the UK data were compared with data from the other studies in Table 7. As noted above, other studies were restricted to one blend style of cigarette and significant effects of blend style, and of plain compared to filtered cigarettes, were found in the current study. Therefore, three separate columns for the UK study are presented in this Table. In results presented in the first column, R^2 values from the regression with all cigarettes were included, irrespective of blend style. In the second column R^2 values from the regression with UK Virginia blends only are shown, which gives a more consistent comparison with other studies that only included one blend style. In the third column results are presented after the data from the plain cigarette brand were excluded also.

For the UK study data in column 1, which included results from a mixture of blend styles, nitrogenous compounds in the particulate phase generally gave the lowest R^2 values for correlation with NFDPM whereas NO was the vapour phase constituent that gave the lowest R^2 values for correlation with CO. The correlations in the UK study were improved by the removal of blended products (column 2) and then the non-filtered brand Senior Service from the model (column 3). Thus, the R^2 values from columns 2 and 3 of the UK Study are similar to those reported in the Canadian and Australian Benchmark Studies.

Across all of these studies, it can be seen that particulate phase constituents correlate well with NFDPM yield, and that most analytes associated with the vapour phase correlate better with CO yield. Some of the differences in R^2 values for the same analytes across the studies may be due to measurement variability. For example, Australian brands were not all given to Labstat for analysis at the same time and so long-term within laboratory variability must be considered. Similarly, it is not known whether the Canadian brands were all analysed for each smoke constituent during a short period of time.

Although it is possible only to make general observations across the studies, once again the major cigarette design features that appear to have a noticeable impact on R^2 values were blend type and plain vs. filtered designs. Tobacco-specific nitrosamines gave relatively low correlations with NFDPM in all the studies. The effect of the inclusion of both plain and filtered brands in these studies is also reflected in the relatively low correlations for alkyl phenols. The Canadian Benchmark study included one plain brand, the Massachusetts Benchmark study included two plain brands, but only filtered products were included in the Australian study.

Differences in the reported yields of constituents in different studies: Product, method and measurement variability may contribute a substantial proportion of the observed differences, relative to NFDPM, in the smoke constituent yields across the different studies. To explore this question, three constituents (nitric oxide (NO), B[*a*]P and 1-NA) were chosen and their actual yields from data reported for the Canadian, Australian and UK studies were analysed and are plotted together in Figure 7.

The measured constituent yields all increased with NFDPM yield in each study. At equivalent NFDPM yields, NO yields for the UK cigarettes appeared to be consistently higher than those from either Canada or Australia; whereas for 1-NA, the yields of the UK cigarettes were lower. Both NO and 1-NA are nitrogen-containing constituents and were expected to show consistent patterns with blend style; however, the predominant blend style in all of these countries is Virginia tobacco. It is possible that the relatively higher and lower yields of the respective constituents for UK cigarettes highlights analytical differences between the studies rather than real blend effects. It was also apparent that the B[*a*]P yields were more homogeneous across all three countries. While many trends could be discussed across 40+ constituents and three studies, it is apparent from this brief examination that many inconsistencies may become apparent due to the types of measurement uncertainty discussed above. It is also conceivable that real differences in smoke constituent yield could remain completely undetected, due to measurement uncertainty having an over-riding or masking effect.

Table 7. Comparison of R^2 values across studies

	UK						Australia		Canada		Massachusetts	
Analyte	NFDPM [a]	NFDPM [b]	NFDPM [c]	CO [a]	CO [b]	CO [c]	NFDPM [d]	CO [d]	NFDPM [e]	CO [e]	NFDPM [f]	CO [f]
CO	0.89	0.87	0.96	1.00	1.00	1.00	—	—	—	—	—	—
NFDPM	1.00	1.00	1.00	0.89	0.87	0.96	1.00	0.93	1.00	0.98	1.00	0.70
Nicotine	0.94	0.99	0.99	0.81	0.85	0.93	0.96	0.89	0.90	0.86	0.98	0.64
Acetaldehyde	0.87	0.88	0.94	0.97	0.98	0.98	0.92	0.95	0.95	0.96	0.82	0.92
Acetone	0.89	0.89	0.94	0.97	0.97	0.98	0.89	0.86	0.95	0.95	0.78	0.95
Acrolein	0.84	0.87	0.93	0.91	0.96	0.97	0.90	0.91	0.93	0.94	0.83	0.92
Butyraldehyde	0.89	0.94	0.97	0.92	0.96	0.98	0.87	0.81	0.95	0.95	0.77	0.88
Crotonaldehyde	0.90	0.93	0.94	0.89	0.93	0.97	0.92	0.83	0.91	0.91	0.86	0.86
Formaldehyde	0.69	0.81	0.84	0.72	0.86	0.87	0.95	0.90	0.79	0.79	0.81	0.55
Methyl ethyl-ketone	0.90	0.91	0.94	0.96	0.96	0.98	0.86	0.80	0.94	0.94	0.77	0.93
Propionaldehyde	0.88	0.90	0.94	0.96	0.97	0.97	0.91	0.88	0.93	0.90	0.79	0.93
NO	0.54	0.70	0.75	0.58	0.79	0.79	0.76	0.81	0.91	0.92	0.78	0.89
B[*a*]P	0.82	0.91	0.94	0.79	0.87	0.88	0.94	0.94	0.94	0.91	0.99	0.72
Ammonia	0.37	0.81	0.79	0.32	0.65	0.71	0.96	0.86	0.96	0.95	0.88	0.58
HCN	0.93	0.93	0.95	0.93	0.95	0.97	0.96	0.95	0.92	0.95	0.88	0.87
Pyridine	0.68	0.91	0.92	0.58	0.73	0.90	0.96	0.86	0.94	0.90	0.89	0.63
Quinoline	0.87	0.91	0.92	0.68	0.68	0.84	0.92	0.88	0.90	0.85	0.89	0.42
Styrene	0.92	0.91	0.93	0.91	0.92	0.94	0.90	0.82	0.82	0.80	0.67	0.64
NAB	0.22	0.59	0.56	0.20	0.47	0.55	0.60	0.58	—	—	—	—
NAT	0.38	0.45	0.41	0.33	0.38	0.43	0.89	0.76	0.92	0.89	0.70	0.54
NNK	0.21	0.59	0.59	0.21	0.56	0.57	0.58	0.52	0.91	0.87	0.89	0.73
NNN	0.14	0.25	0.23	0.12	0.18	0.18	0.78	0.65	0.72	0.73	0.67	0.56
Acrylonitrile	0.92	0.93	0.96	0.93	0.94	0.96	0.74	0.65	0.95	0.95	0.59	0.52
Benzene	0.87	0.87	0.94	0.95	0.95	0.95	0.66	0.59	0.95	0.95	0.64	0.81
Isoprene	0.86	0.88	0.94	0.92	0.93	0.94	0.69	0.60	0.94	0.96	0.72	0.73
Styrene	0.89	0.89	0.91	0.90	0.91	0.93	—	—	—	—	—	—
Toluene	0.90	0.89	0.96	0.96	0.95	0.96	0.67	0.59	0.96	0.96	0.66	0.81
1,3-Butadiene	0.86	0.85	0.95	0.97	0.97	0.97	0.68	0.60	0.88	0.91	0.68	0.74
Catechol	0.82	0.95	0.95	0.71	0.80	0.87	0.97	0.91	0.91	0.87	0.86	0.53
Hydroquinone	0.82	0.95	0.95	0.72	0.81	0.86	0.92	0.89	0.93	0.91	0.90	0.68
Phenol	0.61	0.60	0.90	0.31	0.27	0.77	0.91	0.80	0.77	0.73	0.88	0.19
Resorcinol	0.85	0.95	0.97	0.79	0.88	0.91	0.70	0.44	—	—	—	—
m- & p-Cresol	0.73	0.73	0.92	0.46	0.40	0.82	0.92	0.77	0.87	0.84	0.79	0.17
o-Cresol	0.68	0.67	0.92	0.40	0.34	0.81	0.91	0.77	0.84	0.80	—	—
Cadmium	0.34	0.48	0.53	0.35	0.52	0.52	0.81	0.85	0.94	0.93	0.87	0.61
Lead	0.63	0.57	0.62	0.66	0.64	0.64	0.82	0.61	—	—	—	—
Mercury	0.72	0.68	0.71	0.78	0.76	0.76	0.75	0.66	—	—	—	—
1-Naphthylamine	0.65	0.83	0.82	0.55	0.63	0.72	0.56	0.38	0.88	0.85	0.93	0.50
2-Naphthylamine	0.54	0.74	0.72	0.49	0.59	0.65	0.52	0.37	0.89	0.86	0.90	0.60
3-Aminobiphenyl	0.45	0.76	0.75	0.42	0.65	0.69	0.62	0.46	0.90	0.87	0.94	0.65
4-Aminobiphenyl	0.46	0.71	0.69	0.41	0.57	0.63	0.59	0.43	0.85	0.82	0.94	0.65

[a] For the UK study, NFDPM and CO = all brands included.
[b] For the UK study, NFDPM and CO = only products designated as Virginia blend included.
[c] For the UK study, NFDPM and CO = only Virginia blend included, the one plain brand excluded.
[d] Australian brands were all Virginia blend.
[e] Canadian brands were all Virginia blend.
[f] Massachusetts brands were all American blend.

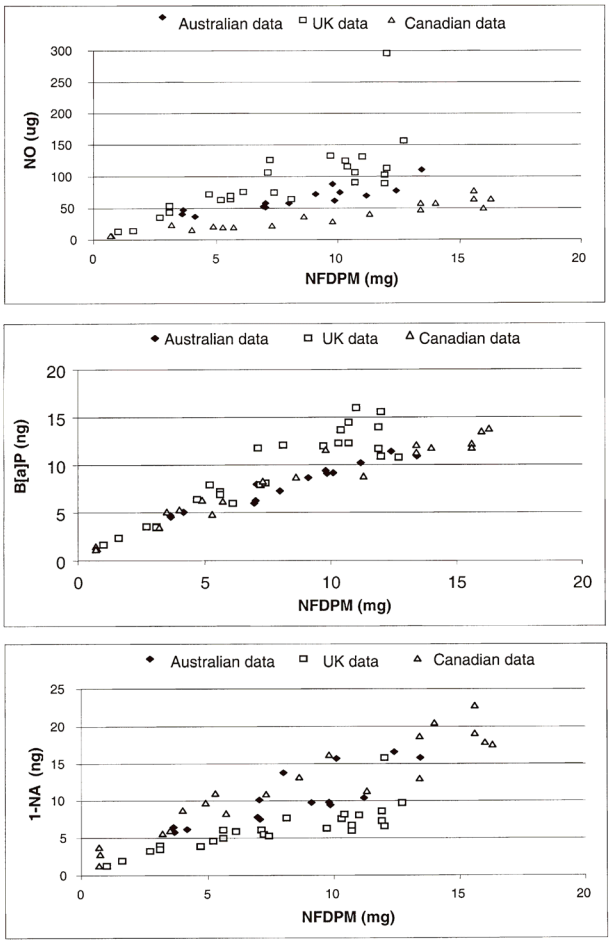

Figure 7. Comparison of the yields of selected constituents across 3 studies

DISCUSSION

This study is one of a number in which the yields of approximately 40 smoke constituents plus NFDPM, nicotine and CO have been determined for contemporary cigarettes. The smoke constituents on the list are based on previously published lists evolved from the HOFFMANN Group (6) and Health Canada, who funded the development of the methods within Labstat. In the Australian, Canadian and Massachusetts studies (11,12,13,31) single blend styles of cigarettes were analysed, reflecting the predominance of discrete blends in those markets, and functional relationships between NFDPM, nicotine and CO were established for each study. In the present study, three blend styles were included in the analysis.

Across all studies, NFDPM or CO yields were very good indicators of other constituent yields. This is demonstrated by the good R^2 values seen for the majority of smoke constituents in each study. For the UK study slightly lower R^2 values were found for a number of analytes, although all remained statistically significant. Based on the improvement in R^2 values by excluding American blended products, it is likely that the mixture of UK Virginia, American blend and dark air-cured blend styles in one study accounts for the lower R^2 values but a contribution from the analytical methods and measurement uncertainty cannot be excluded.

The possible contribution to variation in smoke constituent yield of cigarette design features was examined in the current study using simple regression analysis techniques, a normalised smoke constituent yield regression model, and multiple regression techniques. With the exception of blend and presence of a filter, it is concluded that other design features used in cigarettes on sale in the UK have only a minor relative effect on smoke constituent yield variability, other than any direct effect that they have on NFDPM yield. The same design features were included in the Australian, Canadian and Massachusetts Benchmark studies, which also reported good correlations with NFDPM yields. From these data, it is concluded that for standard cigarettes the impact of cigarette design features other than blend and presence of a filter, on smoke constituents yields, is minor and secondary to any effect that is produced on NFDPM yield.

Across all of these studies, the measurement of some smoke constituents proved to be problematic. For example, trace metals were always at or near their limits of detection and were not detected in all brands. This is unsurprising because metals are not formed by combustion chemistry and their presence in the smoke stream can only reflect a carry over from trace metals in the tobacco crop. Other constituents such as resorcinol and NAB were also near the detection limits for the methods employed.

Because of the recent interest in the topic of smoke constituent yields, a plethora of publications have appeared, leading to a suggestion that measurement of minor smoke constituents can be performed readily and reliably. However, the duration of the current study itself ($\geq$18 months) was mainly due to the time required to establish the assays for minor smoke constituents, even in a contract laboratory with many years of experience in tobacco smoke analysis.

The variability seen in this single-point-in-time sampling study, with many CoV values above 15%, suggests that greater variability for other analytes than the tolerances for NFDPM and nicotine in ISO 8243 would be seen, if such testing for minor smoke constituents became more widespread. The data presented in the comparison of a subset of brands between two contract laboratories in this study, and the comparison of this study with other recent publications questions the current ability to achieve long-term, within-laboratory or between-laboratory consistency. All of these contemporary studies suggest that, if routine measurements of these smoke constituents were to be called for, measurement tolerances typically in excess of 50% and sometimes above 100% might be required, based on current laboratory capability.

In the absence of standardised methods of analysis, comparison of measured yields of smoke constituents across different studies may be of limited value because of difficulties in interpretation. To illustrate this point, data on measured yields from the Australian and Canadian Benchmark studies were compared with those from the current study. As expected, this comparison shows that the blend dependence of some constituent yields, the measurement uncertainty around other constituent yields, and a possible combination of these effects, could lead to large differences in reported yields. Therefore, it seems prudent to regard the results of the studies to date as providing relative yield data within each study rather than absolute data for comparison with those from other studies.

OVERALL CONCLUSIONS

Accumulated data from a number of countries suggest a good relationship between standard cigarettes' NFDPM yields and other smoke constituent yields. Particulate phase constituent yields correlate best with NFDPM yield but volatile constituent yields show better correlation with CO yields. Apart from the known effects of differences in blend style and the difference between filtered or unfiltered ("plain") cigarettes and direct effects on NFDPM and CO yields, cigarette design features have little additional effect on the smoke constituent yields. Thus, taking into account the large experimental variability encountered in the analysis of these smoke constituents, it is suggested that the yields of smoke constituents are largely predictable within the degree of measurement uncertainty, given any standard cigarette's NFDPM and CO yield. Furthermore, routine measurement of smoke constituent yields other than NFDPM, nicotine and CO would not add substantially to the scientific knowledge base.

The analytical variability and unknown tolerances around the measurements encountered in this and other studies suggest that smoke constituents yield data, apart from NFDPM, nicotine and CO yields, are currently not sufficiently robust to develop regulatory standards for the routine analysis of standard cigarette products.

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Address for correspondence

Evan Gregg
Consultant to the Tobacco Manufacturers' Association
Burwood House, 14/16 Caxton Street
London SW1H 0ZB
UK
E-mail: evaneni@aol.com

APPENDIX. Tables A1–A4

Table A1. Cigarette product descriptions

Brand	Company [a]	NFDPM (mg)	Length (mm)	Menthol	Blend style [b]	Weight (g)	Porosity (CU)	Filter dilution (%)	Circum-ference (mm)	Filter type [c]
Silk Cut Ultra	GL	1	84		UKB	0.56	44	82	24.8	CA
L&B Ultra Lights	ITL	1	84		UKB	0.63	71	76	24.9	CA
Silk Cut EM KS	GL	3	84		UKB	0.56	44	69	24.8	CA
Superkings Ultra Lights	ITL	3	99		UKB	0.55	71	57	24.7	CA
Camel Ultra Lights	JTI	3	84		AMB	0.57	50	70	24.9	CA
Silk Cut KS	GL	5	84		UKB	0.64	71	57	24.8	CA
Mayfair Menthol	GL	5	84	Y	UKB	0.58	44	69	24.8	CA
L&B Lights KS	ITL	5	84		UKB	0.58	44	42	24.9	CA
Marlboro Lights	PM	6	84		AMB	0.62	34	45	24.8	CA
Red Band Lights	REE	6	84		UKB	0.61	60	51	24.8	CA
Vogue Super Slims	BAT	7	99		AMB	0.38	20	45	17.0	CA
Consulate Menthol	BAT	8	84	Y	UKB	0.63	50	30	24.8	CA
Mayfair Lights KS	GL	8	84		UKB	0.63	44	30	24.8	CA
Superkings Lights	ITL	8	99		UKB	0.68	44	31	24.7	CA
Rothmans Royals	BAT	11	84		UKB	0.67	50	23	24.8	CA
B&H KS	GL	11	84		UKB	0.65	29	17	24.8	CA
Berkeley SK	GL	11	99		UKB	0.73	71	19	24.8	CA
Regal Filter	ITL	11	71		UKB	0.53	44	7	24.7	CA
Gitanes Caporal	ALT	12	70		DAC	0.68	15	14	26.7	CA
Senior Service	GL	12	69		UKB	0.74	200	0	25.1	NF
L&B KS	ITL	12	84		UKB	0.63	44	0	24.6	CA
Superkings	ITL	12	99		UKB	0.73	71	0	24.7	CA
Regal KS	ITL	12	84		UKB	0.62	44	0	24.7	CA
Marlboro KS	PM	12	84		AMB	0.77	54	19	24.8	CA
Rothmans Royals 120s	BAT	12	120		UKB	0.76	75	25	22.0	CA

[a] Manufacturers: ALT = Altadis; BAT = British American Tobacco, GL = Gallaher Limited; ITL = Imperial Tobacco Limited; JTI = Japan Tobacco International; PM = Philip Morris; REE = Reetsma (now part of ITL).
[b] Blend style: UKB = typical UK Virginia blend; AMB = typical American blend; DAC = dark air-cured.
[c] Filter type: CA = cellulose acetate; NF = non-filtered.

Table A2. Individual smoke constituents yields (summary) [a,b]

	NFDPM mg/cig		CO mg/cig		Nicotine mg/cig		Cadmium ng/cig		Lead ng/cig		Mercury ng/cig		Nickel ng/cig		Arsenic ng/cig		Selenium ng/cig		Chromium ng/cig		HCN µg/cig	
Brand	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV
Benson & Hedges KS	10.30	4.33	11.74	4.12	0.84	4.21	19.13	11.99	14.94	3.92	2.60	7.15	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	129.70	11.49
Berkely Superkings	9.69	5.56	11.50	4.92	0.79	4.77	15.78	13.39	17.89	7.66	2.15	4.29	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	119.87	4.81
Camel Ultra Lights	3.09	8.80	3.13	6.14	0.29	3.80	9.18	17.73	2.81	7.15	0.97	8.62	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	20.42	13.76
Consulate Menthol	7.06	4.81	8.30	4.10	0.58	4.81	10.93	16.14	8.87	12.29	1.61	5.05	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	90.37	10.13
Gitanes Caporal Filter	12.00	4.19	12.60	5.09	0.64	3.16	90.34	12.45	23.12	7.42	2.80	5.45	n/a	n/a	4.50	4.47	10.26	12.77	n/a	n/a	127.43	10.96
L&B King Size	11.93	4.62	13.30	3.30	0.86	4.61	34.55	14.17	31.01	9.10	2.65	6.30	n/a	n/a	2.75	—	n/a	n/a	n/a	n/a	141.87	13.73
L&B Lights KS	5.24	6.88	6.48	5.58	0.45	4.87	8.81	19.34	8.34	9.54	1.26	3.41	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	67.89	16.30
L&B Ultra Lights	1.61	10.98	1.49	14.01	0.17	9.99	1.55	10.44	n/a	n/a	0.27	5.25	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	9.57	15.93
Marlboro KS	12.69	3.43	12.79	4.08	0.91	3.62	46.90	16.20	18.79	8.36	2.56	6.16	n/a	n/a	4.44	9.57	n/a	n/a	n/a	n/a	132.46	7.27
Marlboro Lights KS	6.10	5.19	7.19	5.04	0.52	4.73	21.21	14.22	8.07	4.71	1.65	9.01	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	55.80	6.11
Mayfair Lights KS	7.23	5.35	8.73	5.74	0.57	5.27	12.26	7.79	13.99	7.76	1.84	11.25	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	99.50	5.32
Mayfair Menthol KS	4.65	7.61	5.95	5.28	0.42	5.46	7.63	9.84	7.87	8.10	1.26	11.27	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	49.21	4.72
Red Band Lights KS	5.55	7.17	6.41	5.37	0.47	5.54	23.72	5.99	8.00	4.94	2.57	6.59	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	53.85	10.73
Regal Filter	10.65	4.56	10.92	4.49	0.82	3.93	15.50	16.00	15.14	8.85	1.67	6.35	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	113.28	6.44
Regal KS	11.96	4.46	13.86	4.03	0.90	5.01	21.86	19.15	19.30	13.89	2.20	5.88	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	139.39	9.41
Rothman Royals 120s	10.39	4.73	9.44	5.90	0.83	5.43	23.62	14.51	17.14	9.99	2.05	8.98	n/a	n/a	2.85	5.71	n/a	n/a	n/a	n/a	102.58	9.08
Rothman Royals KS	11.00	3.05	10.86	2.84	0.89	3.82	24.05	16.99	17.36	7.86	2.03	3.48	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	134.86	4.57
Senior Service	11.92	6.29	7.71	7.30	0.94	6.13	11.90	6.65	11.10	4.83	1.76	7.28	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	108.50	9.46
Silk Cut Extra Mild	2.67	10.69	3.16	6.77	0.26	6.96	3.13	20.34	2.54	6.25	0.81	5.87	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	24.35	21.92
Silk Cut KS	5.62	6.60	5.78	6.49	0.52	6.77	5.30	4.94	5.51	2.08	1.44	6.24	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	52.78	14.76
Silk Cut Ultra KS	1.01	24.41	1.20	9.81	0.11	9.64	n/a	n/a	n/a	n/a	0.32	15.90	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	8.50	22.23
Superkings	10.71	3.73	11.41	4.61	0.84	5.16	1.64	7.74	2.01	—	2.10	4.68	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	119.95	7.50
Superkings Lights	8.09	4.17	7.54	4.37	0.70	3.91	10.67	9.48	12.14	8.23	1.40	2.31	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	69.77	11.45
Superkings Ultra Lights	3.08	7.51	3.53	6.91	0.26	5.06	4.98	4.75	3.03	15.46	0.84	1.93	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	34.93	19.66
Vogue Superslims	7.38	3.87	6.05	4.16	0.62	2.91	16.33	5.45	15.21	6.29	1.73	4.30	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	90.92	19.52

Table A2 (*cont.*)

	1-NA ng/cig		2-NA ng/cig		3-ABP ng/cig		4-ABP ng/cig		NAB ng/cig		NAT ng/cig		NNN ng/cig		NNK ng/cig		Acetone µg/cig		Formaldehyde µg/cig		Acetaldehyde µg/cig	
Brand	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV
Benson & Hedges KS	7.63	12.16	5.15	8.20	1.11	11.36	0.86	19.08	6.96	10.39	53.01	10.74	31.79	7.30	41.96	8.16	307.37	7.38	28.08	14.11	720.02	8.07
Berkely Superkings	6.32	10.87	4.56	16.19	1.01	16.64	0.80	18.05	7.68	5.02	59.84	9.10	39.49	15.74	46.61	6.39	303.04	6.42	27.44	6.31	705.15	6.32
Camel Ultra Lights	4.03	7.98	2.24	8.33	0.58	4.93	0.51	5.95	3.16	13.05	23.39	11.19	15.44	13.31	22.91	12.38	83.11	13.28	3.97	25.41	167.38	12.14
Consulate Menthol	6.05	9.30	3.50	4.42	0.85	15.47	0.63	5.71	3.82	10.40	25.45	6.31	28.05	20.74	25.97	5.54	216.85	9.09	25.49	17.60	514.46	9.61
Gitanes Caporal Filter	15.79	4.56	10.29	8.04	2.87	9.38	2.06	11.31	44.17	6.49	148.29	9.11	257.56	4.91	499.85	5.06	303.43	9.54	15.44	10.30	686.56	8.33
L&B King Size	7.33	4.78	3.81	14.13	0.99	15.79	0.71	21.79	5.77	4.83	32.02	8.84	29.52	20.82	21.12	8.45	317.74	8.03	52.29	7.30	758.00	7.00
L&B Lights KS	4.60	14.20	2.77	8.73	0.72	9.02	0.54	11.84	2.57	12.47	18.15	22.96	17.19	19.60	12.54	19.61	202.06	4.39	19.32	9.08	462.97	3.31
L&B Ultra Lights	1.95	8.05	1.36	14.62	0.33	10.90	0.28	9.51	1.08	20.44	7.80	17.30	6.62	12.10	5.23	17.11	55.92	14.26	1.81	36.72	108.46	15.77
Marlboro KS	9.69	10.23	5.55	9.74	1.54	8.00	1.21	13.71	12.39	11.48	86.83	10.44	84.27	5.47	105.03	3.63	311.20	3.74	29.73	4.90	715.89	4.04
Marlboro Lights KS	5.93	7.06	4.22	4.63	0.90	8.97	0.73	13.33	5.46	20.21	43.24	16.30	29.36	9.22	44.82	8.82	174.63	2.06	12.53	17.18	401.86	2.88
Mayfair Lights KS	5.45	15.72	3.94	18.39	0.92	10.34	0.74	16.49	8.68	10.80	66.36	14.56	43.81	21.21	58.74	6.02	228.88	9.41	19.23	8.06	519.93	8.50
Mayfair Menthol KS	3.89	7.23	2.65	11.39	0.62	8.32	0.49	13.60	4.08	5.29	33.35	13.28	23.10	17.51	30.62	6.80	159.53	5.74	10.27	10.89	349.11	4.83
Red Band Lights KS	5.04	15.93	2.85	16.84	0.71	17.94	0.57	9.58	2.19	14.06	16.11	7.75	13.56	14.65	11.72	17.80	154.00	8.88	12.13	14.26	350.76	7.86
Regal Filter	5.99	7.43	3.26	10.10	0.81	19.95	0.59	12.56	5.65	3.95	30.45	13.42	25.08	6.45	21.75	13.22	266.46	5.31	39.16	15.65	630.87	4.91
Regal KS	6.58	13.81	3.38	12.34	0.84	14.82	0.63	14.60	5.23	10.69	31.53	5.90	30.22	19.46	22.80	17.02	359.64	7.79	56.31	9.09	872.10	9.59
Rothman Royals 120s	8.15	10.73	4.79	14.91	1.16	9.98	0.87	15.79	7.67	13.62	48.93	11.04	36.30	13.08	74.32	10.48	249.94	4.93	22.46	5.80	566.64	4.10
Rothman Royals KS	8.13	8.73	5.05	10.02	1.08	6.90	0.81	9.59	7.01	6.56	47.04	7.27	49.16	8.12	67.75	9.09	288.58	2.97	36.62	21.23	660.53	3.15
Senior Service	8.64	10.83	4.93	4.21	1.05	6.78	0.88	10.64	8.24	1.68	57.00	4.46	33.57	3.89	44.04	7.46	237.20	6.07	28.56	8.48	523.06	6.31
Silk Cut Extra Mild	3.25	15.00	1.89	19.37	0.52	7.38	0.41	3.67	2.45	12.23	14.81	10.59	11.62	21.26	13.00	14.57	87.99	11.69	4.51	32.96	182.95	12.77
Silk Cut KS	6.06	17.06	3.16	26.37	0.89	8.71	0.71	12.15	3.80	16.32	27.60	9.09	19.85	12.84	17.89	7.35	170.55	8.10	10.06	7.22	367.03	6.40
Silk Cut Ultra KS	1.34	15.78	0.86	15.75	0.22	15.16	0.21	11.15	1.52	7.74	10.23	8.41	6.54	7.79	7.86	16.88	39.08	5.41	1.26	22.81	72.98	5.06
Superkings	6.70	7.84	4.02	11.06	0.92	15.44	0.77	25.67	5.27	18.20	36.82	8.52	33.36	25.81	22.67	11.57	327.78	5.36	46.21	10.07	778.25	3.41
Superkings Lights	7.70	11.06	4.58	7.15	0.97	8.35	0.78	5.92	4.33	13.40	29.66	3.73	23.38	3.17	17.57	8.87	218.41	5.00	22.28	17.14	505.44	5.42
Superkings Ultra Lights	3.53	12.00	2.05	11.17	0.57	9.02	0.47	7.79	4.66	10.08	27.39	15.97	24.34	17.02	39.08	7.49	117.75	5.28	6.13	19.29	267.52	4.46
Vogue Superslims	5.32	10.99	2.61	12.86	0.69	5.68	0.65	9.46	6.59	5.57	48.18	7.27	26.20	4.55	58.91	13.13	151.78	9.93	25.46	13.74	345.90	10.30

Table A2 (*cont.*)

	Quinoline µg/cig		Pyridine µg/cig		Ammonia µg/cig		B[*a*]P ng/cig		Benzene µg/cig		Toluene µg/cig		Isoprene µg/cig		1,3-Butadiene µg/cig		Acrylonitrile µg/cig		Styrene µg/cig		NO µg/cig	
Brand	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV
Benson & Hedges KS	0.28	8.03	7.45	10.95	5.06	12.84	12.26	19.34	43.14	7.12	74.00	5.05	355.52	6.83	33.15	9.47	8.86	8.42	7.22	23.84	124.50	6.47
Berkely Superkings	0.24	6.55	6.53	13.32	1.24	17.24	12.00	21.46	43.50	11.68	71.02	11.38	314.94	9.82	32.28	11.63	8.55	12.59	6.09	6.11	133.38	5.50
Camel Ultra Lights	0.09	42.35	1.19	33.16	5.80	11.18	3.63	18.20	17.43	5.68	23.89	9.40	130.27	7.14	11.85	7.71	2.08	13.80	1.84	32.51	43.38	9.53
Consulate Menthol	0.22	4.27	3.72	10.73	3.24	20.60	11.77	18.81	35.31	8.55	57.96	9.14	264.36	4.84	25.46	6.15	6.56	9.59	4.45	6.38	106.69	5.36
Gitanes Caporal Filter	0.44	9.38	21.29	27.46	18.81	14.98	10.87	11.97	55.84	6.01	100.68	6.01	304.78	5.00	37.44	5.41	13.23	5.88	9.53	25.32	295.56	6.32
L&B King Size	0.28	6.59	9.40	16.99	5.02	8.33	14.04	16.12	51.62	5.17	87.20	6.62	350.26	4.62	39.93	2.50	10.90	5.86	8.61	14.92	102.43	9.56
L&B Lights KS	0.18	13.30	3.26	14.19	2.66	13.64	7.88	25.21	33.06	13.67	54.79	13.44	259.71	10.58	25.62	9.40	5.93	14.15	4.07	12.20	62.61	5.00
L&B Ultra Lights	0.06	63.75	0.98	71.93	0.28	62.02	2.36	23.69	6.66	8.21	8.58	7.31	48.86	8.86	5.58	10.92	0.89	10.27	1.09	59.78	14.08	25.06
Marlboro KS	0.31	3.51	9.31	12.18	8.28	16.55	9.88	20.65	49.05	6.96	93.02	8.22	417.14	6.39	35.58	6.05	10.94	11.10	8.13	9.44	156.62	6.88
Marlboro Lights KS	0.17	19.70	2.62	24.72	3.92	17.66	6.02	13.18	28.31	7.11	44.78	6.09	258.78	5.51	23.38	3.96	4.50	9.52	3.03	21.37	76.88	4.18
Mayfair Lights KS	0.22	6.98	5.27	12.27	4.01	12.78	7.91	17.14	32.66	4.66	55.87	5.03	244.14	8.03	24.89	6.61	7.02	4.55	5.36	7.87	126.69	4.68
Mayfair Menthol KS	0.11	29.37	1.85	21.24	2.13	24.84	6.40	30.03	22.45	5.20	35.14	5.60	175.10	6.49	18.26	5.65	3.55	7.23	2.45	10.92	71.82	10.63
Red Band Lights KS	0.12	26.94	1.96	31.01	2.43	14.56	7.18	14.05	32.50	10.84	48.87	13.67	197.03	9.02	22.25	11.72	5.36	18.26	2.49	25.00	63.88	8.62
Regal Filter	0.26	5.45	8.76	24.50	4.39	14.80	12.28	10.24	43.98	5.53	75.18	8.62	326.42	5.37	34.13	8.01	9.66	4.65	6.93	36.60	90.90	6.12
Regal KS	0.27	11.07	9.54	16.19	5.38	16.33	15.61	23.65	57.54	4.32	97.74	5.82	368.85	5.04	42.20	1.79	11.71	9.83	9.70	2.01	112.69	5.54
Rothman Royals 120s	0.30	4.05	5.75	10.74	5.51	13.22	13.65	14.56	40.11	5.06	69.18	4.38	301.60	2.71	29.41	9.22	7.97	1.68	5.82	6.82	116.30	7.23
Rothman Royals KS	0.34	4.82	8.37	6.46	5.03	16.20	15.97	15.65	48.00	3.54	82.76	6.14	360.99	4.38	35.49	6.14	9.61	4.06	7.70	4.55	131.86	9.24
Senior Service	0.39	5.00	11.14	11.18	5.40	14.74	11.67	15.92	33.73	3.19	59.57	4.34	259.28	5.43	23.13	7.69	8.10	8.33	6.52	7.05	89.02	5.92
Silk Cut Extra Mild	0.07	16.70	1.01	13.46	1.04	26.08	3.64	24.09	16.59	3.64	22.78	3.76	119.10	3.95	12.08	8.40	2.11	6.75	1.47	10.70	35.26	6.89
Silk Cut KS	0.16	17.35	2.86	18.70	2.64	7.74	6.85	13.70	26.32	12.20	41.16	9.38	189.77	9.53	17.53	13.06	4.38	13.82	3.31	13.44	70.28	14.41
Silk Cut Ultra KS	0.01	229.85	0.83	74.28	0.07	181.49	1.68	32.67	6.25	4.47	7.56	5.88	50.30	8.79	4.66	5.02	0.76	15.34	0.93	66.82	13.65	18.79
Superkings	0.25	21.60	8.36	16.59	5.15	10.19	14.48	21.87	52.40	11.60	90.38	13.24	386.96	8.70	37.12	6.80	11.42	12.52	8.25	19.20	106.11	5.88
Superkings Lights	0.22	13.35	3.94	12.52	3.64	22.43	12.10	12.53	37.62	6.19	59.22	4.87	266.15	5.28	27.12	5.71	6.93	5.75	4.42	7.87	64.15	3.93
Superkings Ultra Lights	0.08	25.43	1.61	18.40	1.69	23.49	3.54	19.62	17.16	12.15	25.66	10.79	133.51	14.46	13.14	15.39	2.50	13.81	2.04	10.09	54.06	7.05
Vogue Superslims	0.25	3.70	6.94	5.63	4.56	10.66	8.07	24.09	24.26	4.44	42.82	5.38	203.18	5.27	18.89	3.46	6.43	4.02	4.93	4.79	75.29	5.36

Table A2 (*cont.*)

Brand	Propionaldehyde µg/cig		Butyraldehyde µg/cig		MEK µg/cig		Acrolein µg/cig		Crotonaldehyde µg/cig		Phenol µg/cig		*o*-Cresol µg/cig		*m*- & *p*-Cresol µg/cig		Hydroquinone µg/cig		Catechol µg/cig		Resorcinol µg/cig	
	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV	Mean	CoV
Benson & Hedges KS	52.58	9.86	44.35	8.54	83.28	6.77	59.91	8.44	24.43	9.99	15.91	10.06	4.02	8.94	10.03	8.76	52.86	5.42	57.83	6.38	1.18	3.04
Berkely Superkings	50.82	5.61	40.88	13.14	80.86	7.13	59.60	7.94	23.86	6.11	12.93	5.56	3.48	5.70	8.53	4.62	43.68	1.41	55.11	3.03	1.06	3.65
Camel Ultra Lights	12.82	12.87	9.61	11.83	18.66	13.75	12.38	16.50	3.15	19.51	2.08	10.47	0.69	6.95	1.81	8.90	17.34	11.44	19.73	6.88	0.38	7.15
Consulate Menthol	37.61	10.91	30.53	17.23	56.83	9.38	46.00	13.77	16.61	12.98	11.70	22.32	3.03	19.81	7.35	18.98	42.10	9.42	48.68	6.93	0.90	9.35
Gitanes Caporal Filter	46.75	19.51	36.60	14.74	83.24	9.02	45.78	10.17	22.24	5.54	23.39	5.34	6.50	9.84	15.63	8.78	35.81	4.79	43.89	4.39	0.77	4.13
L&B King Size	54.41	7.05	45.96	9.17	88.83	10.05	69.12	10.53	29.14	5.37	17.09	9.55	4.27	7.78	10.24	8.56	60.72	7.13	67.56	7.30	1.47	7.54
L&B Lights KS	33.73	5.04	26.30	8.01	55.12	5.93	39.09	3.79	14.25	7.68	8.75	17.66	2.27	15.02	5.57	14.58	32.61	14.88	38.08	14.39	0.71	17.00
L&B Ultra Lights	8.18	14.29	8.35	12.34	13.14	12.69	6.42	20.34	2.13	13.23	1.98	16.41	0.61	14.20	1.50	13.70	11.31	8.34	14.01	8.14	0.17	8.68
Marlboro KS	52.91	3.79	42.52	8.75	82.42	4.01	61.67	3.01	22.74	7.79	14.53	4.00	3.83	6.11	9.67	5.46	47.24	5.03	50.22	3.71	1.24	4.18
Marlboro Lights KS	29.60	3.23	19.27	3.22	41.84	2.68	34.41	5.07	8.85	9.45	5.00	11.12	1.37	9.44	3.88	8.47	31.46	4.55	31.61	4.17	0.77	3.49
Mayfair Lights KS	36.98	8.98	32.29	8.34	61.86	10.46	44.32	9.39	17.56	11.61	10.96	10.98	3.09	9.79	7.42	9.30	33.92	3.50	40.36	4.97	0.77	3.68
Mayfair Menthol KS	25.50	5.34	18.95	9.16	40.35	6.69	27.33	7.40	8.66	6.25	5.51	4.10	1.56	4.13	4.07	3.77	25.39	4.30	31.12	2.61	0.52	5.60
Red Band Lights KS	25.19	7.88	24.04	10.58	38.19	9.82	28.28	9.26	8.75	14.81	7.61	9.34	1.78	9.34	5.10	7.27	35.68	3.64	44.22	4.57	0.73	3.97
Regal Filter	45.09	4.88	39.07	3.94	75.02	7.04	57.41	15.31	24.01	7.02	15.77	2.15	3.83	3.22	9.11	2.59	50.14	3.83	55.24	3.57	1.14	5.06
Regal KS	62.06	9.91	51.17	8.26	98.49	7.79	87.76	10.49	33.25	12.22	15.02	4.80	3.69	5.67	9.08	5.09	62.74	4.76	67.61	5.18	1.46	3.87
Rothman Royals 120s	42.23	4.46	37.63	7.33	65.11	4.99	50.84	5.72	19.21	6.99	19.63	8.29	4.60	9.79	11.21	9.16	62.35	6.43	66.66	6.76	1.32	6.14
Rothman Royals KS	48.59	3.25	42.50	4.77	76.95	2.57	62.43	11.08	25.79	4.03	21.65	4.71	4.84	5.96	11.72	5.54	61.81	6.11	70.66	5.53	1.41	5.26
Senior Service	40.57	6.68	36.89	6.34	69.08	5.74	45.95	6.72	24.35	6.10	46.20	9.84	10.00	9.25	21.65	8.75	58.60	4.54	70.60	4.64	1.18	5.75
Silk Cut Extra Mild	13.34	13.93	10.63	16.52	21.23	12.95	12.83	18.84	3.80	16.58	2.89	10.00	0.87	8.35	2.21	8.39	16.96	5.74	19.85	5.80	0.32	5.41
Silk Cut KS	27.07	8.15	23.12	16.79	44.69	10.80	28.72	5.04	10.46	13.51	11.27	15.69	2.89	12.06	6.97	11.16	32.26	3.73	37.30	4.37	0.59	3.14
Silk Cut Ultra KS	5.65	5.54	5.53	12.02	8.25	6.81	4.34	8.35	1.31	7.09	0.91	36.14	0.27	56.85	0.78	31.91	8.46	8.13	10.11	6.33	0.13	8.71
Superkings	56.88	5.31	45.77	2.75	90.66	6.01	69.00	0.78	27.86	7.39	15.85	16.31	4.15	12.11	10.17	11.41	63.21	4.36	69.28	3.96	1.46	5.04
Superkings Lights	37.56	6.35	31.52	4.96	57.97	4.19	43.42	9.27	14.91	10.38	14.10	13.52	3.68	11.24	8.94	10.34	48.48	4.39	57.63	4.51	1.02	2.84
Superkings Ultra Lights	19.63	5.17	16.82	10.98	29.22	5.78	20.07	10.18	6.63	7.30	3.07	14.35	0.96	10.92	2.49	10.15	22.02	7.22	20.98	7.14	0.42	6.81
Vogue Superslims	25.26	10.04	18.30	12.89	38.41	9.57	35.14	11.17	14.24	9.76	14.65	8.89	3.25	6.55	8.42	5.91	30.91	8.73	38.62	6.66	0.93	9.95

[a] n/a = not applicable.
[b] — in CoV columns represent too few results for calculation.

Table A3. Multiple regression analysis of cigarette design features: illustrative examples

Constituent	Step	Parameter entered	Partial R^2	Total R^2	Significance level
Butyraldehyde	0	NFDPM	0.887	0.89	<.0001
	1	Blend style	0.056	0.94	<.0001
	2	Paper porosity	0.018	0.96	0.0287
	3	Circumference	0.013	0.97	0.0163
NAT	0	NFDPM	0.379	0.38	0.0365
	1	Blend style	0.360	0.74	0.0003
Toluene	0	NFDPM	0.902	0.90	<.0001
	1	Paper porosity	0.038	0.94	0.0094
	2	Circumference	0.022	0.96	0.0172
Catechol	0	NFDPM	0.823	0.82	<.0001
	1	Blend style	0.107	0.93	0.0014
NO	0	NFDPM	0.544	0.54	0.0006
	1	Blend style	0.186	0.73	0.0028
Ammonia	0	NFDPM	0.370	0.37	0.0007
	1	Blend style	0.454	0.82	<.0001
HCN	0	NFDPM	0.931	0.93	<.0001
	1	Paper porosity	0.015	0.95	0.0350
	2	Blend style	0.013	0.96	0.0403
o-Cresol	0	NFDPM	0.677	0.68	<.0001
	1	Paper porosity	0.167	0.84	0.0015
Phenol	0	NFDPM	0.607	0.61	0.0001
	1	Paper porosity	0.235	0.84	0.0003
1-Naphythylamine	0	NFDPM	0.652	0.65	0.0001
	1	Blend style	0.173	0.82	0.0004

Stepwise selection of tobacco blend style, menthol (presence or absence), paper porosity, cigarette circumference, cigarette weight and cigarette length was performed for the illustrated smoke constituents yields regressed against NFDPM yield. Only those parameters with a significant effect ($p < 0.05$) are shown.

Table A4. Sources of analytical variability encountered in the UK benchmark study (for abbreviations see Tables 1 and 2)

Area of interest	Specific item	Example of method where the effect may have been observed
General sources of variability	a) Operator to operator variability	a) —
	b) Background contamination	b) acetone, trace metals
	c) Variation in ambient conditions	c) —
	d) Purity of standards	d) —
	e) Suitability of analysis equipment to do the task (e.g. outdated or old equipment)	e) —
Product variability	Measuring the analyte yields from small numbers of cigarettes may make the measurement atypical	carbonyls, HCN
Smoke generation	a) Cross-contamination from sidestream smoke with ventilated products	a) ammonia
	b) Perturbation in the puff-profile, including time-lag in the generation of the smoke due to the pressure drop of the trap arrangement	b) carbonyls, semi-volatile compounds, HCN
Smoke trapping	a) Incomplete trapping of the analyte due to practical compromises in the trap design	a) carbonyls, ammonia, VOCs, mercury
	b) Incomplete trapping of the analyte due to partitioning of compounds between particulate and gas phases	b) VOCs
	c) Change in trapping efficiency with loading for analytes from cigarettes of different yields	c) —
	d) Variability in the trapping efficiency of solid bed adsorbents due to packing inconsistencies	d) HCN, semi-volatile compounds
	e) Potential for contamination from the trapping unit	e) glass tubes and electrostatic precipitator electrode in trace metals analysis
	f) Potential for poisoning or overload of solid phase trapping media for high yield products	f) —
Analyte derivatisation, clean-up and concentration	a) Poor recoveries in the clean-up and concentration steps. Numerical errors introduced through use of recovery standards to multiply and compensate for yields	a) —
	b) Variable recoveries near to 100% where no recovery standard is used	b) B[*a*]P
	c) Difficulties in removing/extracting all of the analyte from the trapping system	c) HCN, aromatic amines
	d) Difficulty in analysis due to the effects of the “dirty-matrix” of cigarette smoke degrading machine performance over short time intervals	d) TSNA by GC-TEA (method abandoned during study)
Analyte reactivity in the detection process	Variable timing between generation and analysis for time-sensitive analyses	NO, ammonia, HCN
Interference during detection	a) Co-elution or lack of complete chromatographic separation	a) —
	b) Interference between artefacts and the analyte	b) polyatomic complexes in trace metals
	c) Interference from co-reacting species	c) quenching or enhancing effects from CO or alkenes in NO analysis
Non-specific detection	a) Non-specific detection in non-chromatographic or mass spectrometry-based detection	a) colorimetric methods for HCN
	b) Separation of peaks into isomeric forms	b) acetaldehyde
	c) Need to have all analytes in the system in the same specific condition for analysis	c) metals analysis – acid concentration and oxidation state
Calibration errors	a) Matrix interference in the detection of an analyte, or in the internal standard, invalidating the calibration or analysis	a) B[*a*]P, polyatomic complexes in metals analysis
	b) Yields outside of calibration range requiring additional analytical steps for some samples to bring the solution into the calibration range	b) semi-volatile compounds
	c) Difficulties in simultaneously calibrating for different members of an analysis group due to different phases	c) gas or liquid phase – 1,3-butadiene in the VOC method
	d) Intercepts on regression lines introducing significant errors in the yields from low yield products	d) several
Low sensitivity of the detector	a) Method insufficiently sensitive for the deliveries from low yield brands	a) ammonia, HCN
	b) Changes in number of cigarettes or trapping method required to compensate for this	b) several
	c) Poor resolution or precision for one member of an analysis group	c) NNK in TSNA by GC/TEA (method abandoned during study)
	d) Analysis machines working close to their “limit of operation” thereby affecting precision of measurement	d) metals