Current Measurement Reliability of Selected Smoke Analytes*

by

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SUMMARY

The reliability of measurements of mainstream smoke analytes other than "tar", nicotine and carbon monoxide (CO) is not known but is important in the current regulatory environment internationally. An appreciation of between laboratory variability is essential for companies contracting analytical work to outside suppliers.

Seven laboratories obtained data from three cigarette brands for as many as they could currently measure of the 44 smoke analytes, commonly referred to as the "Hoffmann list". The brands, of "tar" yields 12 mg, 8 mg and 5 mg, were smoked under the International Organisation for Standardisation (ISO) smoking regime to obtain average yield values based on 5 replicates, each laboratory smoking their chosen number of cigarettes per replicate. In addition, laboratories used their preferred and internally validated methodology i.e. smoking machine type, trapping system, sample work-up and detection system. Around 3600 data points were obtained.

This study was based on one point in time measurements. It did not therefore include any components of longer-term variability that would be expected to further increase the measurement variability. No analytes had lower within-laboratory measurement variability than "tar" and 70% of the other analytes had significantly higher levels. All laboratories ranked the products in the same order for all analytes (except some metals) but there were as much as 10-fold differences in measured values between laboratories. The mean difference between highest and lowest yield measurements was 80% when the values for the three smoke analytes with differences in excess of 8-fold were excluded.

Given the lack of standardised methods, and the consequent high degree of inter-laboratory variability it is not currently possible to make meaningful comparisons between such data from several sources. Indeed, calculation of yields from benchmarking studies may prove no less reliable. [Beitr. Tabakforsch. Int. 20 (2003) 314–324]

ZUSAMMENFASSUNG

Die Zuverlässigkeit der Messungen der wichtigsten Rauchanalyten des Hauptstromrauchs außer Kondensat, Nikotin und Kohlenmonoxid (CO) ist nicht bekannt, spielt jedoch im gegenwärtigen regulativen Umfeld international eine wichtige Rolle. Eine Bewertung der Messabweichungen zwischen verschiedenen Untersuchungslabors ist wichtig für Unternehmen, die derartige Analysen extern vergeben.

Sieben Untersuchungslabors ermittelten von drei Zigarettenmarken Daten so vieler Substanzen aus der Liste der 44 Rauchinhaltsstoffe, die als „Hoffmann"-Liste bekannt ist, wie es ihnen möglich war zu messen. Die Marken mit einem Kondensatgehalt von 12 mg, 8 mg und 5 mg wurden gemäß ISO-Norm abgeraucht. Die Mittelwerte basierten auf 5 Wiederholungsmessungen, wobei jedes Untersuchungslabor die von ihm gewünschte Anzahl Zigaretten pro Messung abrauchte. Darüber hinaus benutzten die Labors ihre jeweils bevorzugte und intern validierte Methodik bezüglich Rauchmaschinentyp, Auffangsystem, Probenaufbereitung und Detektionssystem. Ungefähr 3600 Einzeldaten wurden ermittelt.

Die Studie basierte auf einem Messzeitpunkt. Aus diesem Grund ist die Studie nicht dazu angelegt, längerfristige Schwankungen zu untersuchen, von denen zu erwarten wäre, dass sie die Messabweichungen zusätzlich weiter erhöhen. Bei keinem Analyt war die laborinterne Varianz geringer als bei Kondensat, und bei 70% der anderen Analyten waren die Abweichungen signifikant erhöht. Alle Labors klassifizierten die Zigarettenmarken für alle Rauchanalyte (außer einiger Metalle) in derselben Rangfolge, dennoch variierten die Messwerte in den verschieden Labors mitunter um das Zehnfache. Die mittlere Abweichung zwischen den höchsten und niedrigesten gemessenen Werten betrug 80%, wenn die Werte für drei Analyten mit mehr als 8-fachem Unterschied ausgeschlossen wurden.

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Aufgrund fehlender standardisierter Methoden und den hieraus resultierenden Abweichungen zwischen den Ergebnissen verschiedener Labors ist es gegenwärtig nicht möglich, aussagekräftige Vergleiche zwischen solchen Werten aus unterschiedlichen Quellen anzustellen. Die Berechnung von Hauptstromrauchwerten aus „Benchmarking"-Studien könnten sich als ebenso unzuverlässig erweisen. [Beitr. Tabakforsch. Int. 20 (2003) 314–324]

RESUME

La fiabilité des mesures des analytes de la fumée du courant principal autres que le goudron, la nicotine et le monoxyde de carbone (CO) n'est pas connue, mais elle est importante à l' échelle internationale dans le contexte réglementaire actuel. L' appréciation de la variabilité des mesures entre les laboratoires est indispensable pour les sociétés confiant des travaux analytiques aux laboratoires extérieurs.
Sept laboratoires ont obtenu des données relatives à la fumée de trois marques de cigarettes pour 44 analytes de la fumée, généralement appelés "Liste Hoffmann" pour autant qu' ils pouvaient mesurer à l' époque. Les marques dont les teneurs en goudron étaient de 12 mg, 8 mg et 5 mg, ont été fumées selon la norme ISO pour obtenir des teneurs moyennes basées sur 5 répétitions, chaque laboratoire fumant un nombre choisi de cigarettes par répétition. De plus, les laboratoires ont appliqué leur méthodes préférées et validées, c' est-à-dire type de machine à fumer, système de piégeage, préparation des échantillons et système de détection. Près de 3600 données ont été recueillies.
Cette étude est basée sur des mesures uniques. Par conséquent, l' étude n' examine pas de variations à plus long terme, dont on pourrait s' attendre à une augmentation supplémentaire de l' imprécision de la mesure. Parmi tous les analytes, la variation intralaboratoire du taux de goudron s' avère la plus petite, et pour 70% des autres analytes une variation significative peut être observée. Tous les laboratoires ont classé les produits dans le même ordre pour tous les analytes (sauf certains métaux), néanmoins les valeurs mesurées varient d'un facteur 10 entre laboratoires. La différence moyenne entre les mesures des teneurs les plus et les moins élevées est de 80%, lorsque 3 valeurs en excès d' un facteur de 8 sont exclues.
Etant donné l' absence de méthodes normalisées, et le degré élevé de variation entre laboratoires qui en résulte, il n' est pas possible actuellement de faire des comparaisons significatives entre de telles données provenant de plusieurs sources. En fait, le calcul des teneurs provenant d'études de référence pourrait s' avérer non moins fiable. [Beitr. Tabakforsch. Int. 20 (2003) 314–324]

INTRODUCTION

The reliability of measurements of mainstream smoke analytes other than "tar", nicotine and carbon monoxide (CO) is not known but is important in the current international regulatory environment. An appreciation of between laboratory variability is essential for companies involved in selecting laboratories for measurements or in comparing product data gathered from different laboratories.

Previous "benchmarking" studies have coped with between laboratory variability either by distributing analyte measurements so that particular laboratories measure particular analytes (1), or by using one laboratory for all analyte measurements, irrespective of the representative nature or quality of the data it generates (2).
Very few publications are available giving inter-laboratory comparisons although HSU *et al.* recently reported a series of cigarette analyses and method validation (3). They concluded that for these laboratories adopting their own protocols, differences of greater than 30% were found in smoke yields.
The present study compares smoke data generated at different laboratories when testing cigarettes from a common sample. It measures the inter-laboratory variability between up to seven laboratories for a series of three Imperial Tobacco Limited cigarette products designed at three different "tar" levels and containing mainly flue-cured tobaccos.
It should be noted that the study design eliminated both longer-term product and testing variability, both of which would be expected to increase the overall variability in these measurements.

METHODS

Three cigarette products produced during July or August 2000 were supplied to the laboratories for the smoke analyses, which were carried out between September 2000 and July 2001. These cigarette products contained essentially flue-cured tobacco and their designs covered a range of "tar" values i.e. 12 mg (Product A), 8 mg (Product B) and 5 mg (Product C). Matched samples were used in this work to reduce product variability to a minimum.
Two non-tobacco industry contract laboratories and two tobacco manufacturers' laboratories carried out extensive smoke analyses on the 44 smoke analytes commonly referred to as the "Hoffmann list". In addition, another tobacco manufacturer's laboratory and two non-tobacco industry laboratories were able to measure some of the selected smoke analytes at the time of the study.
Currently there are no internationally recognised standard methods for these analytes, apart from "tar", nicotine and carbon monoxide (CO). For each smoke analyte, each laboratory used whichever smoking machines (linear or rotary), trapping systems and analytical methodology *their* experts considered best and used as part of their normal practice. Each laboratory also applied their internal validation process. A summary of the analytical methods employed at each laboratory and the number of cigarettes smoked per determination for the different methods is given in Table 1.
It was recognised that this selection method would better reflect the current state of analytical expertise despite potentially increasing variability. Some recognised sources of variability are the smoking machine type and set-up, smoke trapping efficiencies, puff profile changes when trapping into liquid traps, sample work-up, instrument measurements, interference from other smoke components and calibration standards.
Cigarettes were conditioned in compliance with ISO 3402 (4) and smoked following the requirements of ISO 3308 (5)

Table 1. Summary of the main features of the analytical methods

Analytes[a]	Laboratory code[b, c]						
	A	B	C	D	E	F	G
"Tar", nicotine and CO; 3	Linear smoker (5) ISO methods	Linear smoker (5) ISO methods	Rotary smoker (20) ISO methods	Linear smoker (5) ISO methods	Linear smoker (5) ISO methods	Linear smoker (5) ISO methods	Linear smoker (5) ISO methods
Carbonyls; 7	Linear smoker (2) DNPH[d] derivative HPLC WS	Linear smoker (3–7) DPAIH[e] derivative HPLC WS	Linear smoker (3-6) DNPH[d] derivative HPLC WS	Linear smoker (2) DNPH[d] derivative HPLC WS	N/A[f]	Linear smoker (8) Colorimetric and GC-MS WS	Linear smoker (1) DNPH[d] derivative HPLC WS
Phenols; 7	Linear smoker (5) HPLC PP	Linear smoker (5) HPLC PP	Linear smoker (5) HPLC PP	Linear smoker (5) HPLC PP	Linear smoker (7) CEC PP	Linear smoker (5) HPLC PP	Linear smoker (5) HPLC PP
Benzo[*a*]pyrene; 1	Linear smoker (5) HPLC PP	Linear smoker (5) HPLC PP	Rotary smoker (20) GC-MS PP	Linear smoker (5) HPLC PP	Linear smoker (5) GC-MS PP	Linear smoker (5) HPLC PP	Linear smoker (5) HPLC PP
Aromatic amines; 4	N/A[f]	Rotary smoker (1) Derivatised GC-MS (SIM) WS	Rotary smoker (20) Derivatised GC-MS (SIM) WS	Rotary smoker (10) Derivatised GC-MS (SIM) WS	N/A[f]	N/A[f]	Rotary smoker (5) Derivatised GC-MS (SIM) WS
Nitric oxide; 1	N/A[f]	10 channel smoker (10) CL VP	8 channel smoker (8) CL VP	Single port smoker (1) CL VP	Rotary smoker (10) CL VP	N/A[f]	Linear smoker (1) CL VP
Hydrogen cyanide; 1	Linear smoker (5) IC WS	Linear smoker (5) Colorimetric WS	Linear smoker (5) ISE VP	Linear smoker (5) Colorimetric VP + PP	N/A[f]	Linear smoker (3) Colorimetric WS	Linear smoker (3) Colorimetric WS
Ammonia; 1	Linear smoker (5) IC PP	Linear smoker (5) Colorimetric WS	Linear smoker (5) IC WS	Rotary smoker (10) IC PP + VP	N/A[f]	N/A[f]	Linear smoker (5) WS HPLC / Conductivity
Vapour phase components; 6	N/A[f]	Rotary smoker (20) GC-MS (SIM) VP/PP	Rotary smoker (20) GC-MS (SIM) VP/PP	Rotary smoker (10) GC-MS (SIM) VP/PP	Rotary smoker (20) GC-MS VP	Linear smoker (8) GC-MS VP	Linear smoker (5) GC-MS (SIM) VP/PP
Semi-volatile bases; 2	Linear smoker (10) PP + VP GC-MS (SIM)	Rotary smoker (20) GC-MS (SIM) PP + VP	Rotary smoker (20) GC-MS (SIM) PP+VP	Rotary smoker (20) GC-MS (SIM) PP + VP	N/A[f]	Linear smoker (5) GC-MS (SIM) WS	Linear smoker (5) GC-MS (SIM) PP + VP
Metals; 7	Linear smoker (8–20) AAS WS	Rotary smoker (40) ICP-MS & AAS WS	Rotary smoker (20) AAS WS	Rotary smoker (20-40) AAS WS	N/A[f]	N/A[f]	Rotary smoker (20) ICP-MS + AAS WS
Nitrosamines; 4	N/A[f]	Rotary smoker (10) GC-TEA PP	Rotary smoker (20) GC-TEA PP	Rotary smoker (10-12) GC-TEA PP	N/A[f]	N/A[f]	Linear smoker (5) HPLC-MS-MS PP

[a]Figures in analytes column refer to the number of smoke analytes measured.
[b]Figures in brackets give the number of cigarettes smoked per replicate.
[c]Abbreviations: WS = whole smoke collected; PP = smoke collected on filter pad; VP = smoke collected beyond the filter pad in various traps;
IC = ion chromatography; ICP = inductively coupled plasma; HPLC = high performance liquid chromatography; GC = gas chromatography; IS = ion selective electrode; CL = chemi-luminescence; TEA = thermal energy analyser; MS = mass spectroscopy; SIM = single ion monitoring; AAS = atomic absorption spectrometry; CEC = capillary electro chromatography, ISE = ion selective electrode.
[d]DNPH = 2,4-dinitrophenylhydrazone.
[e]DPAIH = 2-diphenylacetyl-3-indandione-1-hydrazine
[f]N/A = not analysed.

Table 2. Smoke analyte mean smoke yields – Product A

Analytes	Units	Laboratory code							Mean
		A	B	C	D	E	F	G	
NFDPM[a]	mg/cig	12.4	12.0	12.4	12.6	12.2	12.7	14.0	12.6
Nicotine	mg/cig	1.03	0.98	1.20	1.05	1.00	1.03	0.98	1.04
Carbon monoxide	mg/cig	14.2	13.6	16.2	14.0	15.3	13.3	15.6	14.6
Benzo[*a*]pyrene	ng/cig	11.1	11.6	9.8	14.8	15.5	9.6	13.2	11.4
Nitric oxide	µg/cig	—	128.3	127.8	136.3	122.6	—	176.4	138.3
Hydrogen cyanide	µg/cig	160	170	124	149	—	183	143	157
Ammonia	µg/cig	6.2	16.6	11.1	12.9	—	—	7.5	11.7
Benzene	µg/cig	—	54.5	51.6	45.3	44.1	60.8	64.5	53.5
Toluene	µg/cig	—	72.1	83.2	67.0	65.3	68.6	106.4	77.1
Styrene	µg/cig	—	6.0	23.8	9.8	2.4	—	13.2	11.1
1,3-Butadiene	µg/cig	—	76.5	21.9	50.7	—	—	40.3	47.4
Isoprene	µg/cig	—	470	394	337	364	489	352	401
Acrylonitrile	µg/cig	—	13.4	16.2	9.0	12.2	15.0	13.5	13.9
Quinoline	µg/cig	0.5	0.5	0.4	0.4	—	1.4	0.3	0.6
Pyridine	µg/cig	11.1	5.5	11.8	12.1	—	10.4	9.2	10.1
Phenol	µg/cig	16.5	16.2	18.4	18.9	38.1	19.3	18.0	20.8
m/p-Cresol	µg/cig	8.3	11.0	10.8	12.8	8.7	6.4	10.9	9.8
o-Cresol	µg/cig	7.4	3.9	4.2	4.9	2.8	5.4	4.6	4.7
Formaldehyde	µg/cig	67.5	76.5	72.6	59.6	—	61.8	74.4	68.7
Acetaldehyde	µg/cig	843	1111	818	792	—	1036	910	918
Acetone	µg/cig	377	362	368	394	—	373	434	385
2-Butanone	µg/cig	—	102.8	115.4	76.4	—	94.2	168.4	111.5
Propanal	µg/cig	60.4	67.9	68.2	70.9	—	50.2	82.1	66.6
Butanal	µg/cig	29.2	—	61.0	39.8	—	48.8	48.6	45.5
Crotonaldehyde	µg/cig	35.4	33.9	25.7	23.0	—	23.0	45.0	31.0
NNK[b]	ng/cig	—	41.5	35.0	31.6	—	—	31.6	34.9
N-Nitrosonornicotine	ng/cig	—	22.8	16.3	24.2	—	—	20.0	21.1
N-Nitrosoanatabine	ng/cig	—	45.6	34.7	34.5	—	—	26.9	38.3
N-Nitrosoanabasine	ng/cig	—	8.3	<7	3.7	—	—	5.1	6.0
4-Aminobiphenyl	ng/cig	—	1.0	1.3	1.8	—	—	1.3	1.4
3-Aminobiphenyl	ng/cig	—	1.5	1.6	2.5	—	—	1.6	1.8
2-Naphthylamine	ng/cig	—	3.9	8.1	8.5	—	—	7.5	7.0
1-Naphthylamine	ng/cig	—	11.9	12.0	14.1	—	—	11.7	12.4
Resorcinol	µg/cig	1.2	1.3	1.3	0.7	6.7	8.1	1.4	3.0
Hydroquinone	µg/cig	72.2	75.0	81.7	73.7	68.4	83.8	71.3	75.1
Catechol	µg/cig	74.3	76.5	83.1	71.5	60.5	56.3	78.9	71.6
Chromium	ng/cig	12.4	<5	<2	5.0	—	—	2.5	6.6
Cadmium	ng/cig	23.3	23.7	40.2	36.8	—	—	29.5	30.7
Lead	ng/cig	22.1	15.5	12.0	29.2	—	—	18.3	19.4
Mercury	ng/cig	3.4	2.0	0.4	4.1	—	—	—	2.5
Nickel	ng/cig	<2	<6	<3	4.6	—	—	<2.1	4.6
Selenium	ng/cig	<2	<6	<1.3	1.1	—	—	<0.9	1.1
Arsenic	ng/cig	2.2	1.7	1.1	1.6	—	—	1.8	1.7
Acrolein	µg/cig	—	102.9	48.7	85.9	—	68.8	105.2	76.6
“Smoke pH”		6.0	6.1	5.0	—	—	5.1	—	5.5

[a]NFDPM = nicotine free dry particulate matter (“tar”).
[b]NNK = 4-(*N*-methyl-*N*-nitrosamino)-1-(3-pyridyl)-1-butanone.

as closely as possible. Five replicates were made per analyte. Around 3600 data points were collected during this work. On external statistical advice, four outliers were excluded from the analyses in line with ISO 5725-2 guidelines (6).

This study was based on one point in time measurements and did not include any components of longer-term variability.

DISCUSSION OF RESULTS

A summary of the mean values obtained by each laboratory for each brand is given in Tables 2 to 4.

Puff number

One parameter that might be expected to directly influence the yield of all analytes is the puff number (PN). In addi-

Table 3. Smoke analyte mean smoke yields – Product B

Analytes	Units	Laboratory code							Mean
		A	B	C	D	E	F	G	
NFDPM[a]	mg/cig	7.1	6.8	7.3	7.5	7.4	7.5	8.8	7.5
Nicotine	mg/cig	0.71	0.70	0.87	0.74	0.69	0.70	0.72	0.73
Carbon monoxide	mg/cig	6.8	6.3	7.6	7.0	7.4	6.3	8.0	7.1
Benzo[*a*]pyrene	ng/cig	5.1	5.7	4.4	7.6	8.4	5.0	7.0	5.6
Nitric oxide	µg/cig	—	56.5	56.0	65.0	58.2	—	84.9	64.1
Hydrogen cyanide	µg/cig	68	89	62	65	—	134	90	84
Ammonia	µg/cig	4.2	10.6	7.4	8.6	—	—	5.4	7.7
Benzene	µg/cig	—	28.5	25.5	23.3	21.8	45.8	37.9	30.5
Toluene	µg/cig	—	38.3	45.8	34.6	32.7	52.2	59.9	43.9
Styrene	µg/cig	—	2.8	10.3	4.8	1.3	—	7.0	5.2
1,3-Butadiene	µg/cig	—	34.9	15.1	29.6	—	—	25.8	26.4
Isoprene	µg/cig	—	276	322	235	191	460	281	294
Acrylonitrile	µg/cig	—	6.4	8.2	8.2	4.4	11.6	7.3	7.7
Quinoline	µg/cig	0.4	0.3	0.3	0.3	—	1.1	0.3	0.5
Pyridine	µg/cig	7.0	3.5	6.4	6.4	—	8.3	6.0	6.3
Phenol	µg/cig	14.1	14.3	17.3	13.4	34.1	15.3	14.5	17.6
m/p-Cresol	µg/cig	6.9	9.4	9.7	9.1	6.7	5.3	8.6	8.0
o-Cresol	µg/cig	5.2	3.5	3.5	3.5	2.8	4.3	3.6	3.8
Formaldehyde	µg/cig	34.9	35.8	35.6	30.1	—	40.8	38.1	35.9
Acetaldehyde	µg/cig	466	571	419	414	—	738	521	518
Acetone	µg/cig	231	192	186	214	—	282	272	229
2-Butanone	µg/cig	—	59.3	58.9	43.2	—	71.0	95.8	65.6
Propanal	µg/cig	34.1	36.7	35.3	37.9	—	37.8	48.8	38.4
Butanal	µg/cig	17.3	—	38.6	24.6	—	35.2	29.2	29.0
Crotonaldehyde	µg/cig	17.8	15.5	13.5	10.0	—	18.4	25.1	16.8
NNK[b]	ng/cig	—	30.3	29.0	29.0	—	—	24.8	28.3
N-Nitrosonornicotine	ng/cig	—	19.1	15.4	21.1	—	—	17.1	18.5
N-Nitrosoanatabine	ng/cig	—	36.6	32.0	30.3	—	—	26.1	33.0
N-Nitrosoanabasine	ng/cig	—	7.1	<7	3.3	—	—	3.9	5.2
4-Aminobiphenyl	ng/cig	—	0.7	1.0	1.3	—	—	1.0	1.0
3-Aminobiphenyl	ng/cig	—	1.1	1.1	1.8	—	—	1.3	1.3
2-Naphthylamine	ng/cig	—	2.9	5.4	6.1	—	—	6.0	5.1
1-Naphthylamine	ng/cig	—	7.9	8.4	9.7	—	—	8.4	8.6
Resorcinol	µg/cig	0.7	0.9	0.8	0.6	3.1	5.6	1.0	1.8
Hydroquinone	µg/cig	42.9	49.2	55.1	43.6	46.7	70.9	47.5	50.8
Catechol	µg/cig	43.3	48.0	55.1	41.4	38.9	35.2	49.7	44.5
Chromium	ng/cig	8.7	<5	<2	4.7	—	—	1.9	5.1
Cadmium	ng/cig	20.6	22.2	28.2	35.3	—	—	29.4	27.1
Lead	ng/cig	11.4	8.8	10.4	16.8	—	—	9.4	11.3
Mercury	ng/cig	3.5	1.5	0.4	3.1	—	—	—	2.1
Nickel	ng/cig	<2	<6	<3	5.3	—	—	<2.1	5.3
Selenium	ng/cig	<2	<6	<1.3	0.8	—	—	<0.9	0.8
Arsenic	ng/cig	2.2	2.1	1.9	1.9	—	—	2.0	2.0
Acrolein	µg/cig	49.4	46.8	41.7	42.1	—	49.4	54.0	47.2
"Smoke pH"		6.3	6.3	5.1	—	—	5.4	—	5.8

[a]NFDPM = nicotine free dry particulate matter ("tar").
[b]NNK = 4-(*N*-methyl-*N*-nitrosamino)-1-(3-pyridyl)-1-butanone.

tion, since it is not possible to set the airflow specified in ISO 3308 (5) with some of the trapping systems the PN would be expected to vary more than for normal ISO smoking conditions. Table 5 shows that there were differences in PN of one whole puff within one brand between laboratories for the different groups of analytes. However, the laboratory with the highest PN on one brand did not always give the highest PN on the other brands. High PNs did not necessarily mean that a high yield was obtained. For example, vapour-phase compounds analysed by laboratory D had the highest PN, but gave amongst the lowest yields. Within this data set, it was observed that the effect of PN on yield was likely to be relatively small compared with some of the large yield differences observed between laboratories.

Repeatability (within laboratory variability)

Repeatability (*r*) is reflected in the mean coefficient of variation (CoV) values for each analyte across all products

Table 4. Smoke analyte mean smoke yields – Product C

Analytes	Units	Laboratory code							Mean
		A	B	C	D	E	F	G	
NFDPM[a]	mg/cig	5.0	4.9	5.3	5.4	5.0	5.6	6.0	5.3
Nicotine	mg/cig	0.52	0.52	0.62	0.54	0.51	0.53	0.54	0.54
Carbon monoxide	mg/cig	5.7	5.6	6.7	6.1	6.6	5.8	6.6	6.1
Benzo[*a*]pyrene	ng/cig	4.5	4.8	3.6	7.0	7.6	4.1	7.0	5.0
Nitric oxide	µg/cig	—	59.5	58.5	56.7	53.5	—	85.6	62.7
Hydrogen cyanide	µg/cig	58	55	53	47	—	106	90	64
Ammonia	µg/cig	3.0	7.2	5.1	6.4	—	—	3.9	5.4
Benzene	µg/cig	—	25.9	24.8	20.7	22.2	38.2	31.4	27.2
Toluene	µg/cig	—	33.3	43.3	30.1	31.7	32.0	47.9	36.4
Styrene	µg/cig	—	1.7	7.8	3.8	1.2	—	4.4	3.8
1,3-Butadiene	µg/cig	—	34.6	11.3	25.4	—	—	20.9	23.1
Isoprene	µg/cig	—	260	265	198	203	361	215	250
Acrylonitrile	µg/cig	—	5.6	6.5	3.5	5.9	8.8	5.5	6.1
Quinoline	µg/cig	0.3	0.2	0.2	0.2	—	0.4	0.2	0.2
Pyridine	µg/cig	3.2	2.2	4.4	4.4	—	2.4	3.5	3.4
Phenol	µg/cig	8.6	9.2	9.9	9.5	22.3	9.8	10.3	11.4
m/p-Cresol	µg/cig	4.4	6.5	5.9	6.9	4.5	3.8	6.3	5.4
o-Cresol	µg/cig	3.7	2.4	2.2	2.7	<2	3.1	2.7	2.8
Formaldehyde	µg/cig	23.6	22.4	27.1	17.0	—	31.8	17.8	23.3
Acetaldehyde	µg/cig	433	507	375	367	—	630	428	457
Acetone	µg/cig	231	172	186	201	—	247	230	211
2-Butanone	µg/cig	—	54.1	54.5	37.1	—	61.2	81.6	57.7
Propanal	µg/cig	32.8	32.3	31.9	34.0	—	32.6	39.9	33.9
Butanal	µg/cig	17.1	—	35.9	19.1	—	32.6	24.8	25.9
Crotonaldehyde	µg/cig	17.6	11.9	11.1	8.6	—	14.0	19.9	13.9
NNK[b]	ng/cig	—	19.2	13.6	16.3	—	—	16.9	16.4
N-Nitrosonornicotine	ng/cig	—	12.2	7.1	17.4	—	—	11.1	12.3
N-Nitrosoanatabine	ng/cig	—	22.4	17.0	20.1	—	—	19.4	19.9
N-Nitrosoanabasine	ng/cig	—	5.8	<7	3.1	—	—	2.8	4.4
4-Aminobiphenyl	ng/cig	—	0.6	0.7	1.1	—	—	0.9	0.8
3-Aminobiphenyl	ng/cig	—	1.1	0.9	1.4	—	—	1.0	1.1
2-Naphthylamine	ng/cig	—	2.7	4.6	5.0	—	—	5.2	4.4
1-Naphthylamine	ng/cig	—	6.8	6.7	8.1	—	—	7.2	7.2
Resorcinol	µg/cig	0.6	0.6	0.6	0.4	2.1	3.2	0.7	1.2
Hydroquinone	µg/cig	35.3	36.9	40.5	34.5	33.1	61.2	36.2	39.7
Catechol	µg/cig	37.3	38.2	43.5	35.0	33.4	29.1	41.4	36.9
Chromium	ng/cig	5.7	<5	<2	4.8	—	—	<1.7	5.3
Cadmium	ng/cig	6.4	6.7	10.2	13.3	—	—	10.2	9.4
Lead	ng/cig	7.1	7.0	12.0	22.6	—	—	7.7	11.3
Mercury	ng/cig	5.0	1.8	0.4	2.7	—	—	—	2.5
Nickel	ng/cig	<2	<6	<3	5.2	—	—	<2.1	5.2
Selenium	ng/cig	<2	<6	<1.3	1.0	—	—	<0.9	1.0
Arsenic	ng/cig	1.1	0.8	<0.7	0.8	—	—	<1	0.9
Acrolein	µg/cig	45.1	38.4	30.1	36.6	—	36.8	41.8	38.1
"Smoke pH"		7.0	6.3	5.1	—	—	5.8	—	6.0

[a]NFDPM = nicotine free dry particulate matter ("tar").
[b]NNK = 4-(*N*-methyl-*N*-nitrosamino)-1-(3-pyridyl)-1-butanone.

and for all laboratories (i.e. the full available data set). Yields of four metals (arsenic, selenium, chromium and nickel) were consistently below the quantification limit and were excluded from all the following analyses. The other analytes have been ranked in ascending order of CoV values in Figure 1. Twenty-eight of the 40 analytes studied have a significantly higher variation than "tar" (at the 1% level of significance) as shown by a CoV greater than or equal to 7%. With one or two exceptions, there appeared to be no common factors (e.g. methodology and chemical class) making some analytes more or less variable than others.

The average CoV for all the analyses carried out on the three brands for each laboratory was similar and ranged from 6.4–9.0% except for one laboratory where certain analytes gave much higher variability and increased their mean CoV to 14.3%.

It is recognised that "tar", nicotine and carbon monoxide determined yields are more variable for low "tar" products and this is supported in ISO 8243 (7) by the higher tolerance (the greater of ±1 mg or ±20%) for low "tar" products

Table 5. Comparison of mean puff numbers obtained in different analyses[a]

Analytes	Cigarette product		
	A	B	C
"Tar", nicotine, CO	8.3	7.2	7.0
Metals	8.4	7.3	7.1
Phenols	8.1	7.2	6.8
Tobacco-specific nitrosamines	8.6	7.5	7.4
Carbonyls	8.2	7.3	6.9
Amines	8.4	7.4	7.2
Selected vapour-phase components	8.3	7.3	7.0
Ammonia	8.4	7.2	7.0
Hydrogen cyanide	8.2	7.1	6.9
Nitric oxide	8.5	7.5	7.1
Bases	8.2	7.2	7.0
Benzo[*a*]pyrene	8.2	7.0	6.9

[a]These values represent the mean puffs obtained across all replicates and across all laboratories.

i.e. the lower the "tar" yield the more that it varies. The differences in CoVs between the higher and lower "tar" products are shown in Figure 2. For 31 of the studied 40 analytes, higher CoV values were obtained for the lower "tar" product.

Reproducibility (inter-laboratory variability)

A full statistical test of reproducibility (R) and repeatability (r) would not be meaningful as there is insufficient data and an unbalanced design in this study. However, a less rigorous analysis is available.

For a one point in time "tar" measurement based on 20 replicates, the cigarette sampling method, ISO 8243 (7), sets a 95% confidence limit of 20% for duplicate measurements at a different laboratory corresponding to a possible ratio of 1.2. In this work only 5 replicates were made but the average of 1.21 is not inconsistent with the ISO tolerance.

The ratio of the highest to the lowest yield value between laboratories averaged for the three brands is given in Figure 3. For most analytes these ratios are much higher than for "tar", nicotine and CO and would suggest that higher tolerances would be appropriate for these analytes. The analytes with the highest ratios are generally those that prove the most challenging to the analyst because of their chemical instability or their presence at very low levels where the measurement error will be proportionately greater.

The mean variation between highest and lowest yield measurements was 80% even after excluding 3 values in excess of 8-fold (mercury, resorcinol and styrene). The median variation was 74% for the full 40-analyte data set. There are few obvious links between the levels of variability and the analyte chemistry.

This work suggests that, on average, yield differences measured in different laboratories on analytes other than "tar", nicotine and carbon monoxide need to be greater than 80% in order to be confident of a real difference between products.

Correlation of "tar" and CO with analytes

The mean analyte yields for each brand across all laboratories were plotted against either mean "tar" or CO yields, depending on whether the analyte was associated with the particulate or vapour phase (as indicated in Figures 4 and 5 respectively).

Although there is inter-laboratory variability for each analyte for the three products, within-laboratory comparisons ranked the analyte yields of the three products consistently relative to "tar" or CO yields. Therefore, it was considered valid to combine data from all the laboratories to give the overall lines of correlation with "tar" and CO.

For 3 data points, an R^2 value of 0.85 gives a 75% statistical confidence level for the relationship and an R^2 value of 0.975 gives a 90% confidence level. The R^2 values given in Figures 4 and 5 indicated that all but a few analyte yields were well correlated either with "tar" or with CO yields. The lowest R^2 values were observed for nitrosamines, quinoline, alkyl phenols and some trace metals.

CONCLUSIONS

All laboratories used methods they considered most suitable at the time of study. No analytes had statistically lower within-laboratory measurement variability than "tar", and 70% of the other analytes had statistically higher within-laboratory measurement variability.

All laboratories ranked the products in the same order for all analytes (except some metals) but there was as much as 10-fold difference in measured values between laboratories. The mean variation between highest and lowest yield measurements was 80% even after 3 values in excess of 8-fold were excluded. This must be taken into account when interpreting data. Data from certain laboratories may appear precise with low variability within a data set, but absolute yields may be quite different to those found at other laboratories.

Given the lack of standardised methods, it is not currently possible to make meaningful comparisons between such data from several sources given the degree of inter-laboratory variability displayed in this study. Indeed, calculation of yields from benchmarking studies may prove no less reliable than the current data.

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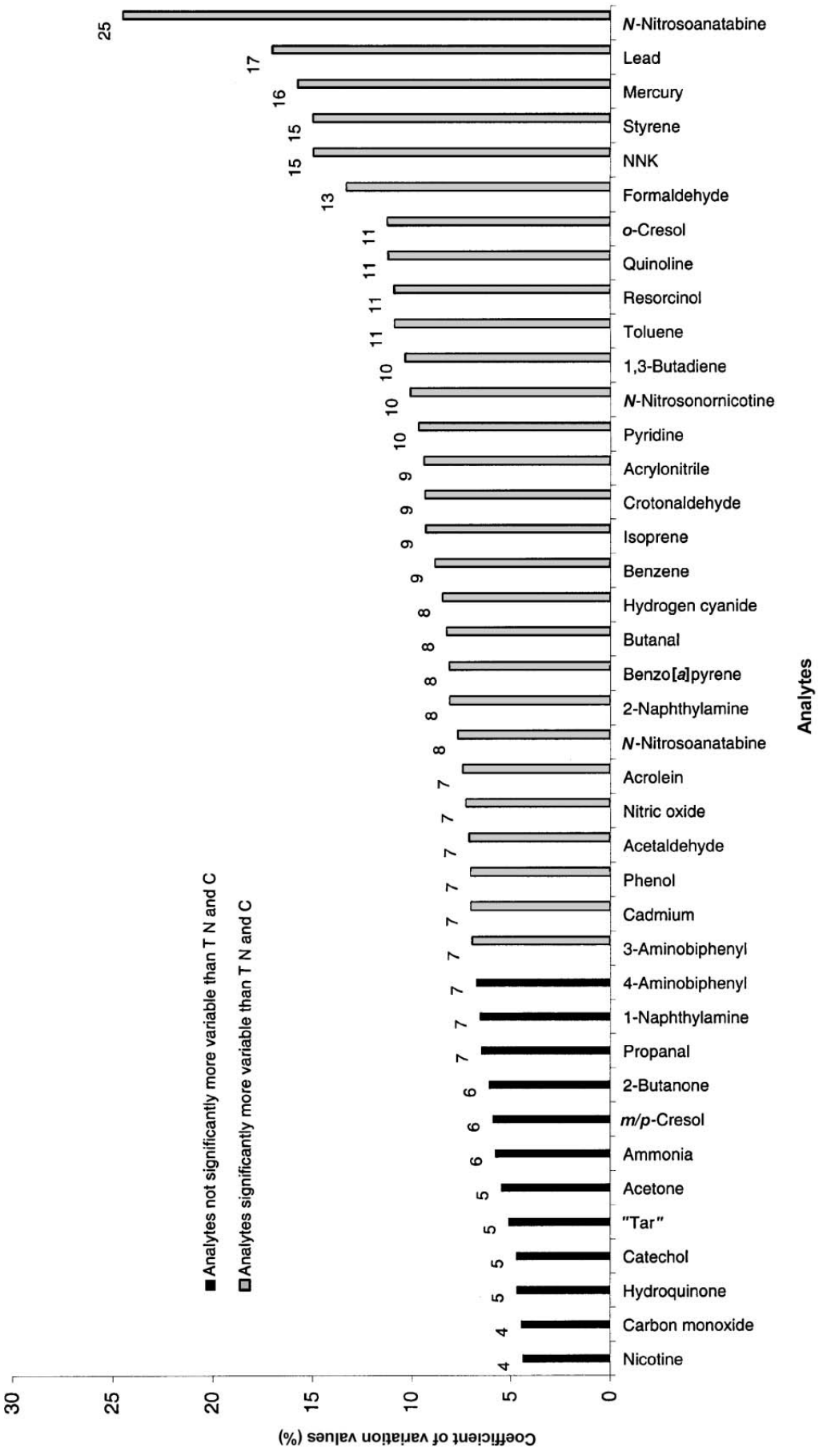

Figure 1. Repeatability (within laboratory variability)

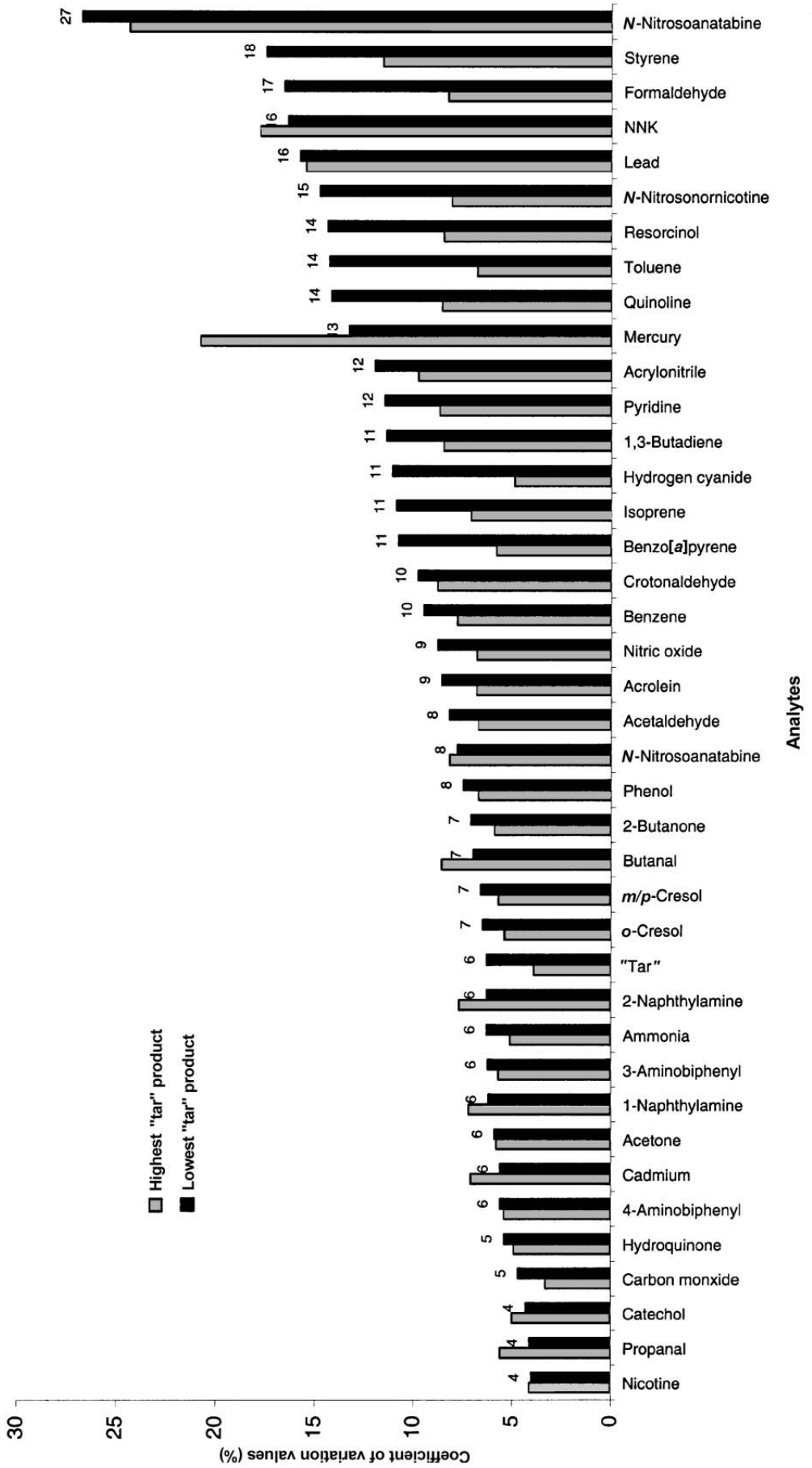

Figure 2. Repeatability (within laboratory variability). Differences between the highest and lowest "tar" products

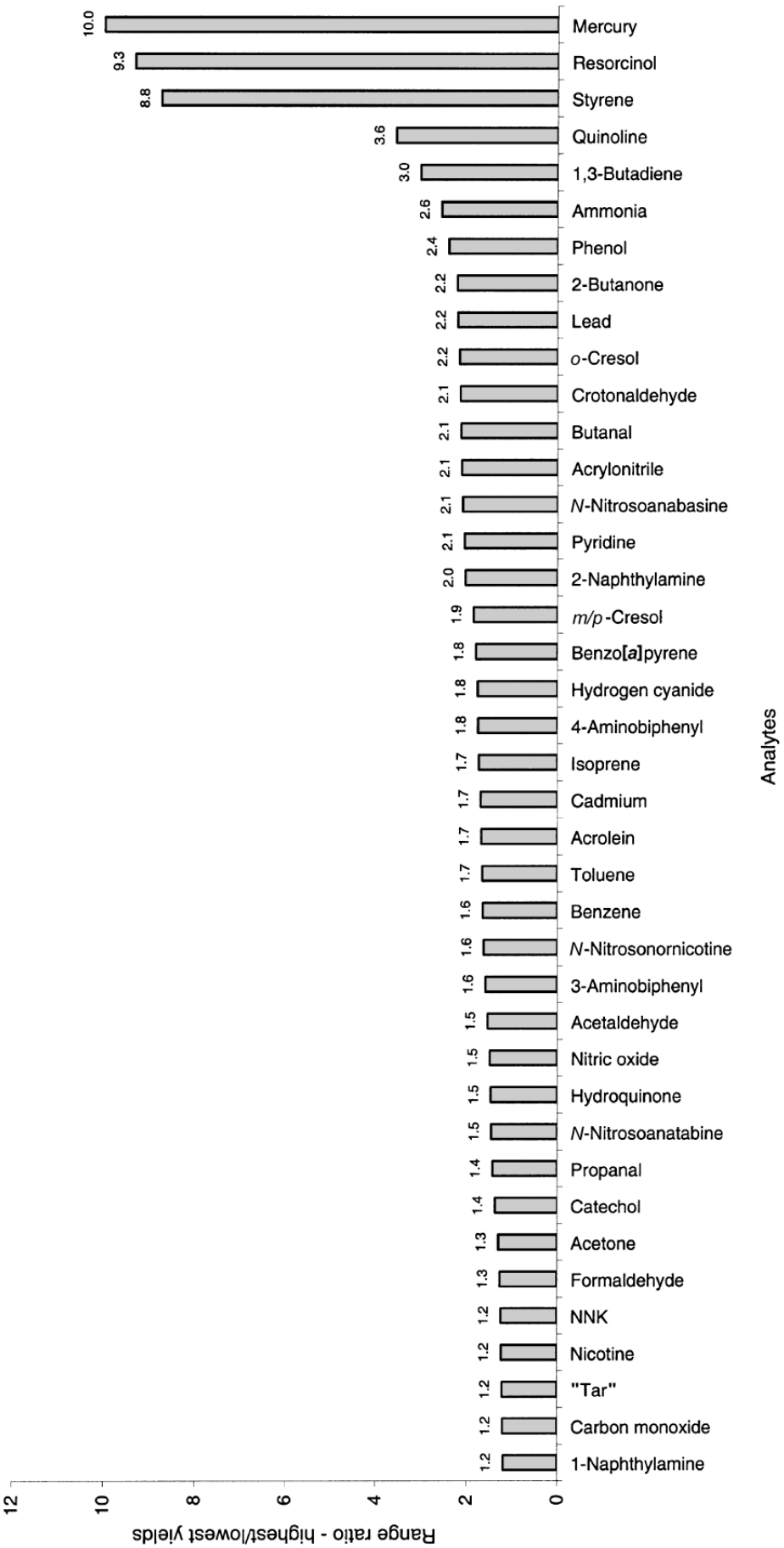

Figure 3. Reproducibility (between laboratory variability). Range ratios of highest to lowest results from laboratories

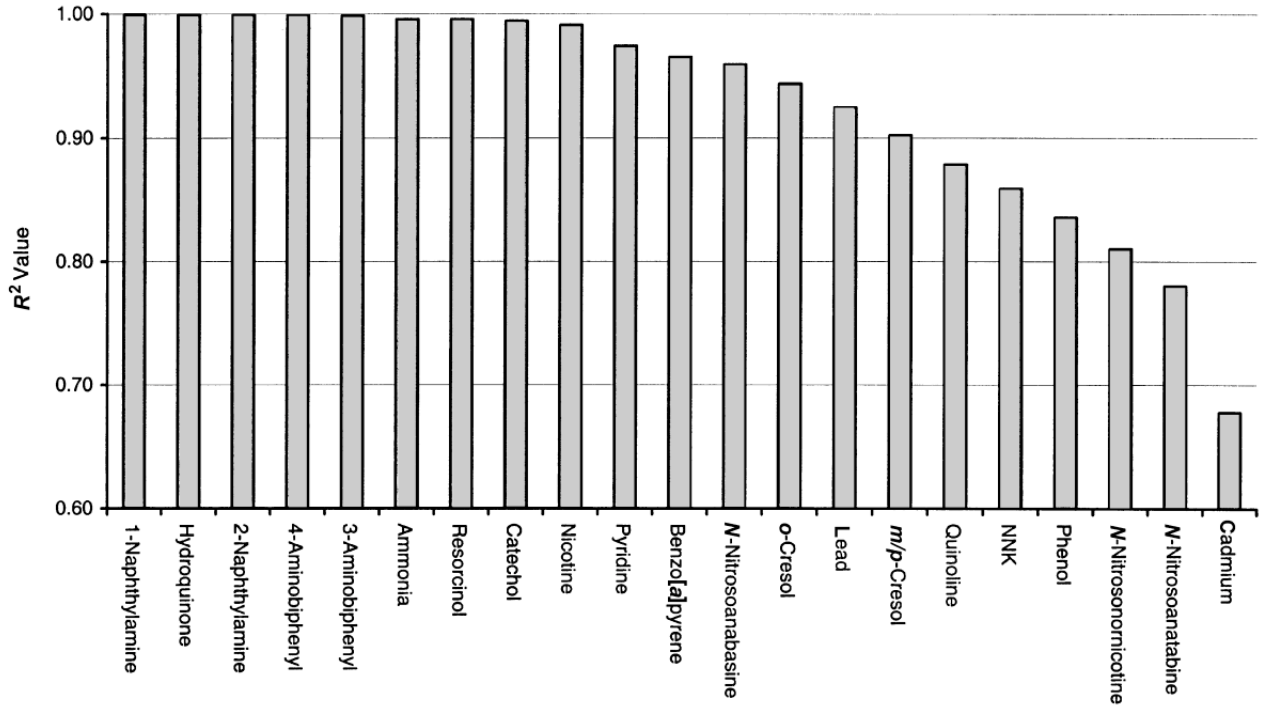

Figure 4. Correlation of analytes with "tar"

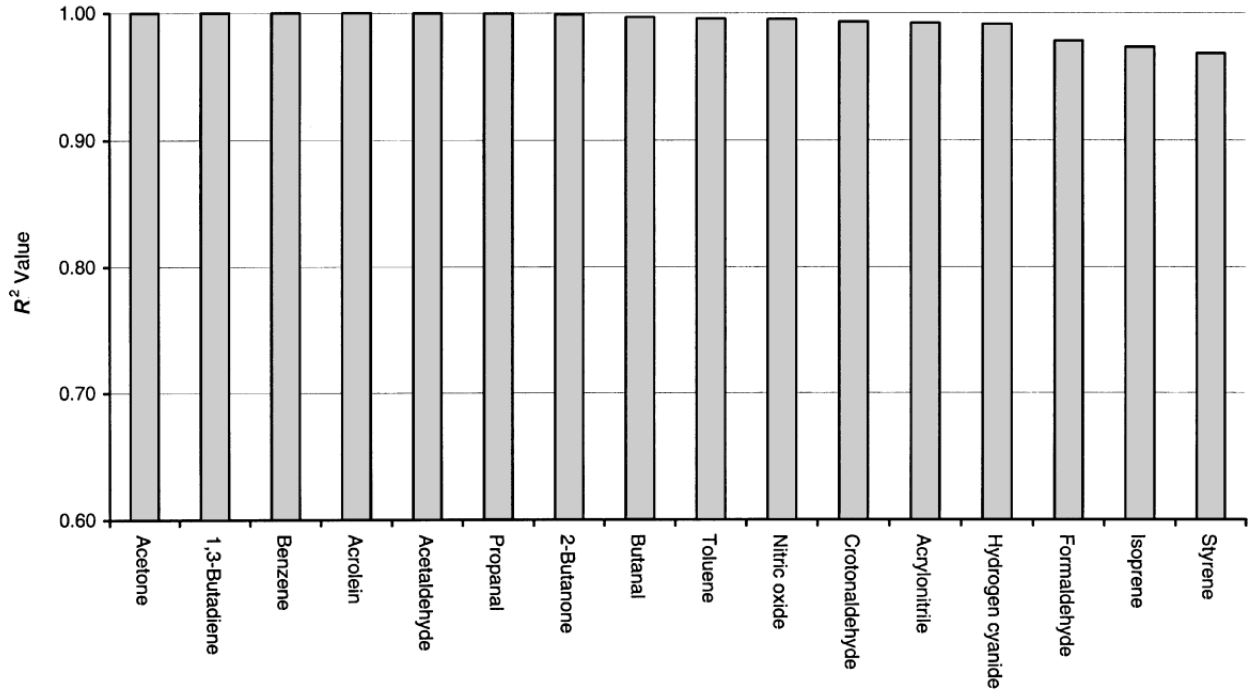

Figure 5. Correlation of analytes with CO

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