CURRENT RELIABILITY OF MEASUREMENTS OF SMOKE ANALYTES

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Abstract

The reliability of measurements of mainstream smoke analytes other than tar, nicotine and 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.

Six laboratories obtained smoke data from three cigarette brands for as many of the 44 'Hoffmann' analytes as they could currently measure. The brands, of tar yields 12mg; 8mg and 5mg, were smoked under the ISO smoking regime to obtain yield values based on 5 replicates, each laboratory using 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 2900 data points were obtained.

This study was based on one-off measurements and did not 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, nicotine and CO and 73% of the other analytes had statistically higher levels. All laboratories ranked the products in the same order for all analytes (except some metals) but there was as much as ten-fold difference in measured values between laboratories. The mean variation between highest and lowest yield measurements was 60% when 3 values in excess of 8-fold were excluded.

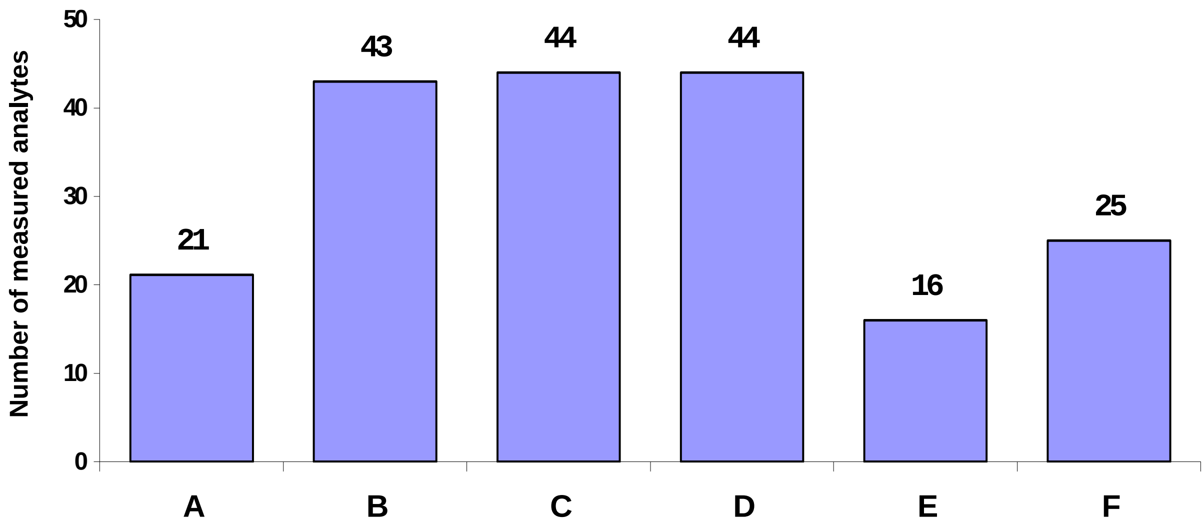
Given the lack of standardised methods, it is not currently possible to make meaningful comparisons between such data from several sources with this degree of inter-laboratory variability. Indeed, calculation of yields from benchmarking studies may prove more reliable.

Study Design

3 commercial brands (containing flue-cured blends) were tested at 6 laboratories (A-F) who measured as many of the 44 Hoffmann smoke analytes as they could using the methods that they consider best.

Product A (12mg tar)
Product B (8mg tar)
Product C (5mg tar)

3 tobacco manufacturers' laboratories and 3 other laboratories received cigarettes from the same batch. Each laboratory has a high level of analytical expertise.



The testing capabilities of the laboratories are given above.

- Five replicates per cigarette type were required for each analyte.
- Around 2900 data points were collected during this work
- Only 4 statistical outliers were excluded from the analyses on advice from external statisticians.

Brief Outline of Analytical Methods

Lab	A	B	C	D	E	F
Tar, nicotine and CO	**Linear (5) ISO**	**Linear (5) ISO**	**Rotary (20) ISO**	**Linear (5) ISO**	**Linear (5) ISO**	**Linear (5) ISO**
Carbonyls		**Linear (3-7) Derivatised HPLC**	**Linear (3-6) Derivatised HPLC**	**Linear (2) Derivatised HPLC**		**Linear (8) Colorimetric & GC/MS**
Phenols	**Linear (5) HPLC**	**Linear (5) HPLC**	**Linear (5) HPLC**	**Linear (5) HPLC**	**Linear (7) CEC**	**Linear (5) HPLC**
BaP	**Linear (5) HPLC**	**Linear (5) HPLC**	**Rotary (20) GC/MS**	**Linear (5) HPLC**	**Linear (5) GC/MS**	**Linear (5) HPLC**
Aromatic Amines		**Rotary (1) Derivatised GC/MS SIM**	**Rotary (20) Derivatised GC/MS SIM**	**Rotary (10) Derivatised GC/MS SIM**		
Nitric Oxide		**Linear (10) CL**	**Linear (8) CL**	**Linear (1) CL**	**Rotary (10) CL**	
HCN	**Linear (5) IC**	**Linear (5) Colorimetric**	**Linear (5) ISE**	**Linear (5) Colorimetric**		**Linear (3) Colorimetric**
Ammonia	**Linear (5) IC**	**Linear (5) Colorimetric**	**Linear (5) IC**	**Rotary (10) IC**		
Vapour phase		**Rotary (20) GC/MS SIM**	**Rotary (20) GC/MS SIM**	**Rotary (10) GC/MS SIM**	**Rotary GC/MS**	**Linear (8) GC/MS**
Bases	**Linear (10) GC/MS SIM**	**Rotary (20) GC/MS SIM**	**Rotary (20) GC/MS SIM**	**Rotary (20) GC/MS SIM**		**Linear (5) GC/MS SIM**
Metals	**Linear (8-20) AAS**	**Rotary (40) ICP MS AAS**	**Rotary (20) AAS**	**Rotary (20-40) AAS**		
TSNAs		**Rotary (10) GC TEA**	**Rotary (20) GC TEA**	**Rotary (10-12) GC TEA**		

Smoking machine shown as linear or rotary with figure in brackets given as the number of cigarettes per replicate.

Even where methods are broadly similar, some differences in protocols are still evident.

Conclusions

- Variability within laboratory of most analytes is significantly greater than for standardised tar measurements, implying the need for greater measurement tolerance.
- Variability between laboratories of most analytes is much greater than tar measurements and is much greater than the within laboratory variability. This does not include the longer-term variability in measurement or product.
- Smoke analyte variability was of the order of 60% between labs and must be taken into account when interpreting data. Data may be precise but precisely wrong.
- Given the lack of standardised methods, it is not currently possible to make meaningful comparisons between analyte data from different laboratories until tolerances have been established.
- ISO Standardisation of all analytes will take a number of years and methods may not be sufficiently precise for routine monitoring. The current viable alternative is benchmarking studies. Indeed, calculation of yields from benchmarking studies may prove no less reliable.

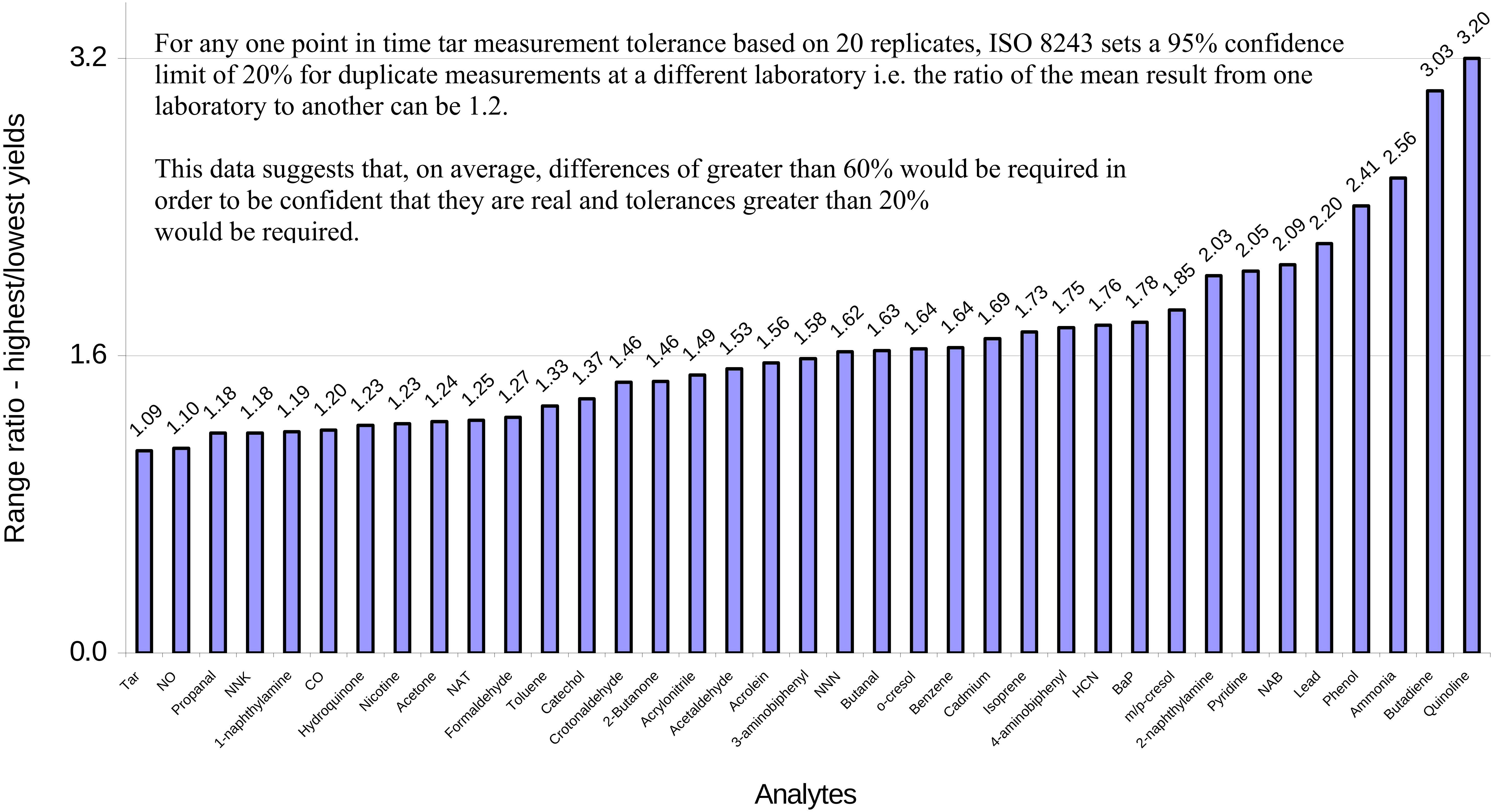
Range Ratios of the highest to lowest yields

The mean yields of the three brands across all laboratories were calculated and the ratio of the highest to the lowest mean yield are given below.

3 analytes gave very high ratios (styrene, resorcinol and mercury) and were excluded from the following analyses. Ratios ranged from 9% for tar to 320% for quinoline.

For any one point in time tar measurement tolerance based on 20 replicates, ISO 8243 sets a 95% confidence limit of 20% for duplicate measurements at a different laboratory i.e. the ratio of the mean result from one laboratory to another can be 1.2.

This data suggests that, on average, differences of greater than 60% would be required in order to be confident that they are real and tolerances greater than 20% would be required.



Mean Analyte Yields for the Three Cigarette Brands

Smoke analyte	Units	Product A							Product B							Product C						
		Lab A	Lab B	Lab C	Lab D	Lab E	Lab F	Mean	Lab A	Lab B	Lab C	Lab D	Lab E	Lab F	Mean	Lab A	Lab B	Lab C	Lab D	Lab E	Lab F	Mean
NFDPM	mg/cig	12.4	12	12.4	12.6	12.2	12.7	12.4	7.1	6.8	7.3	7.5	7.4	7.5	7.3	5	4.9	5.3	5.4	5	5.6	5.2
Nicotine	mg/cig	1.03	0.98	1.2	1.05	1	1.03	1.05	0.71	0.7	0.87	0.74	0.69	0.7	0.73	0.52	0.52	0.62	0.54	0.51	0.53	0.54
CO	mg/cig	14.2	13.6	16.2	14	15.3	13.3	14.4	6.8	6.3	7.6	7	7.4	6.3	6.9	5.7	5.6	6.7	6.1	6.6	5.8	6.1
BaP	ng/cig	11.1	11.6	9.8	14.8	15.5	9.6	12.1	5.1	5.7	4.4	7.6	8.4	5	6	4.5	4.8	3.6	7	7.6	4.1	5.3
NO	ug/cig	-	128.3	127.8	136.3	122.6	-	128.7	-	56.5	56	65	58.2	-	58.9	-	59.5	58.5	56.7	53.5	-	57
HCN	ug/cig	159.7	170	124.4	149.4	-	183	157.3	68	89	62.2	64.6	-	134.2	83.6	58.1	55	52.8	46.8	-	106.4	63.8
Ammonia	ug/cig	6.2	16.6	11.1	12.9	-	-	11.7	4.2	10.6	7.4	8.6	-	-	7.7	3	7.2	5.1	6.4	-	-	5.4
Benzene	ug/cig	-	54.5	51.6	45.3	44.1	60.8	51.2	-	28.5	25.5	23.3	21.8	45.8	29	-	25.9	24.8	20.7	22.2	38.2	26.3
Toluene	ug/cig	-	72.1	83.2	67	65.3	68.6	71.2	-	38.3	45.8	34.6	32.7	52.2	40.7	-	33.3	43.3	30.1	31.7	32	34.1
Styrene	ug/cig	-	6	23.8	9.8	2.4	-	10.5	-	2.8	10.3	4.8	1.3	-	4.8	-	1.7	7.8	3.8	1.2	-	3.6
1,3-butadiene	ug/cig	-	76.5	21.9	50.7	-	-	49.7	-	34.9	15.1	29.6	-	-	26.5	-	34.6	11.3	25.4	-	-	23.8
Isoprene	ug/cig	-	470	394	337	364	489	411	-	276	322	235	191	460	297	-	260	265	198	203	361	257
Acrylonitrile	ug/cig	-	13.4	16.2	9	12.2	15	13.2	-	6.4	8.2	4.4	6.6	11.6	7.4	-	5.6	6.5	3.5	5.9	8.8	6
Quinoline	ug/cig	0.5	0.5	0.4	0.4	-	1.4	0.6	0.4	0.3	0.3	0.3	-	1.1	0.5	0.3	0.2	0.2	0.2	-	0.4	0.3
Pyridine	ug/cig	11.1	5.5	11.8	12.1	-	10.4	10.2	7	3.5	6.4	6.4	-	8.3	6.3	3.2	2.2	4.4	4.4	-	2.4	3.3
Phenol	ug/cig	16.5	16.2	18.4	18.9	38.1	19.3	21.2	14.1	14.3	17.3	13.4	34.1	15.3	18.1	8.6	9.2	9.9	9.5	22.3	9.8	11.6
3/4-methyl phenol	ug/cig	8.3	11	10.8	12.8	8.7	6.4	9.7	6.9	9.4	9.7	9.1	6.7	5.3	7.9	4.4	6.5	5.9	6.9	4.5	3.8	5.3
2-methyl phenol	ug/cig	7.4	3.9	4.2	4.9	2.8	5.4	4.8	5.2	3.5	3.5	3.5	2.8	4.3	3.8	3.7	2.4	2.2	2.7	<2	3.1	2.8
Formaldehyde	ug/cig	-	76.5	72.6	59.6	-	61.8	67.6	-	35.8	35.6	30.1	-	40.8	35.6	-	22.4	27.1	17	-	31.8	24.6
Acetaldehyde	ug/cig	-	1111	818	792	-	1036	939	-	571	419	414	-	738	535	-	507	375	367	-	630	470
Acetone	ug/cig	-	362	368	394	-	373	374	-	192	186	214	-	282	218	-	172	186	201	-	247	201
2-Butanone	ug/cig	-	102.8	115.4	76.4	-	94.2	97.2	-	59.3	58.9	43.2	-	71	58.1	-	54.1	54.5	37.1	-	61.2	51.7
Propanal	ug/cig	-	67.9	68.2	70.9	-	50.2	64.3	-	36.7	35.3	37.9	-	37.8	36.9	-	32.3	31.9	34	-	32.6	32.7
Butanal	ug/cig	-	-	61	39.8	-	48.8	49.9	-	-	38.6	24.6	-	35.2	32.8	-	-	35.9	19.1	-	32.6	29.2
Crotonaldehyde	ug/cig	-	33.9	25.7	23	-	23	26.4	-	15.5	13.5	10.3	-	18.4	14.4	-	11.9	11.1	8.6	-	14	11.4
NNK	ng/cig	-	41.5	35	31.6	-	-	36	-	30.3	29	29	-	-	29.4	-	19.2	13.6	16.3	-	-	16.4
NNN	ng/cig	-	22.8	16.3	24.2	-	-	21.1	-	19.1	15.4	21.1	-	-	18.5	-	12.2	7.1	17.4	-	-	12.3
NAT	ng/cig	-	45.6	34.7	34.5	-	-	38.3	-	36.6	32	30.3	-	-	33	-	22.4	17	20.1	-	-	19.9
NAB	ng/cig	-	8.3	<7	3.7	-	-	6	-	7.1	<7	3.3	-	-	5.2	-	5.8	<7	3.1	-	-	4.4
4-amino biphenyl	ng/cig	-	1	1.3	1.8	-	-	1.4	-	0.7	1	1.3	-	-	1	-	0.6	0.7	1.1	-	-	0.8
3-amino biphenyl	ng/cig	-	1.5	1.6	2.5	-	-	1.9	-	1.1	1.1	1.8	-	-	1.3	-	1	0.9	1.4	-	-	1.1
2-naphthyl amine	ng/cig	-	3.9	8.1	8.5	-	-	6.9	-	2.9	5.4	6.1	-	-	4.8	-	2.7	4.6	5	-	-	4.1
1-naphthyl amine	ng/cig	-	11.9	12	14.1	-	-	12.6	-	7.9	8.4	9.7	-	-	8.7	-	6.8	6.7	8.1	-	-	7.2
Resorcinol	ug/cig	1.2	1.3	1.3	0.7	6.7	8.1	3.2	0.7	0.9	0.8	0.6	3.1	5.6	1.9	0.6	0.6	0.6	0.4	2.1	3.2	1.3
Hydroquinone	ug/cig	72.2	75	81.7	73.7	68.4	83.8	75.8	42.9	49.2	55.1	43.6	46.7	70.9	51.4	35.3	36.9	40.5	34.5	33.1	61.2	40.3
Catechol	ug/cig	74.3	76.5	83.1	71.5	60.5	56.3	70.4	43.3	48	55.1	41.4	38.9	35.2	43.6	37.3	38.2	43.5	35	33.4	29.1	36.1
Chromium	ng/cig	12.4	<5	<2	5	-	-	8.7	8.7	<5	<2	4.7	-	-	6.7	5.7	<5	<2	4.8	-	-	5.3
Cadmium	ng/cig	23.3	23.7	40.2	36.8	-	-	31	20.6	22.2	28.2	35.3	-	-	26.6	6.4	6.7	10.2	13.3	-	-	9.2
Lead	ng/cig	22.1	15.5	12	29.2	-	-	19.7	11.4	8.8	10.4	16.8	-	-	11.8	7.1	7	12	22.6	-	-	12.2
Mercury	ng/cig	3.4	2	0.4	4.1	-	-	2.5	3.5	1.5	0.4	3.1	-	-	2.1	5	1.8	0.4	2.7	-	-	2.5
Nickel	ng/cig	<2	<6	<3	4.6	-	-	4.6	<2	<6	<3	5.3	-	-	5.3	<2	<6	<3	5.2	-	-	5.2
Selenium	ng/cig	<2	<6	<1.3	1.1	-	-	1.1	<2	<6	<1.3	0.8	-	-	0.8	<2	<6	<1.3	1	-	-	1
Arsenic	ng/cig	2.2	1.7	1.1	1.6	-	-	1.7	2.2	2.1	1.9	1.9	-	-	2	1.1	0.8	<0.7	0.8	-	-	0.9
Acrolein	ug/cig	-	102.9	48.7	85.9	-	68.8	76.6	-	46.8	41.7	42.1	-	49.4	45	-	38.4	30.1	36.6	-	36.8	35.5
Smoke pH		6	6.1	5	-	-	5.1	5.5	6.3	6.3	5.1	-	-	5.4	5.8	7	6.3	5.1	-	-	5.8	6

Within laboratory Variability

CoV values are the average of the three brands across all laboratories.

CoV values are quite low for most analytes (~ 9% on average)

The average CoV value for tar is 5%.

23 of the 41 analytes studied have statistically higher CoVs than the standard tar, nicotine and CO analytes at the 1% level of significance.