Results of Proficiency Test Trace Metals in Mouthwash & Toothpaste November 2019

Organised by: Institute for Interlaboratory Studies
Spijkenisse, the Netherlands

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1 INTRODUCTION

Heavy metals like Arsenic, Cadmium, Chromium, Lead, Mercury and Nickel are found in a wide variety of cosmetics or personal care products like lipstick, whitening toothpaste, eyeliner, body cream and foundation. Some metals are intentionally added as ingredients, while others are contaminants. Exposure to metals has been linked to health concerns including reproductive, immune and nervous system toxicity.

In Europe, the current regulation for cosmetics is Council Directive 76/768/EEC. Annex II is a list of substances that cosmetics must not contain like Arsenic, Cadmium, Chromium, Lead and Mercury. Based on this European regulation, China issued the Hygienic Standard for Cosmetics (HSC2007) with limit levels for certain heavy metals in 2007. In 2015, this standard was superseded by the Chinese Technical Safety Standards for Cosmetics (TSSC2015), which was implemented in 2016 (see table 1).

Element	HSC 2007	TSSC 2015
Arsenic	≤10mg/kg	≤2mg/kg
Cadmium	Not Specified	≤5mg/kg
Lead	≤40mg/kg	≤10mg/kg
Mercury	≤1mg/kg	≤1mg/kg

Table 1: Limits for different metals

No reference materials (RMs) for Trace Metals in cosmetics are available to optimise the determination of the metals. As an alternative participation in a proficiency test may enable the laboratories to check their performance and thus to increase the comparability between laboratories.

On request of a number of laboratories, the Institute for Interlaboratory Studies (iis) decided to set up a proficiency test of the determination of Trace Metals in Mouth Wash and Toothpaste during the annual testing program 2019/2020.
In this interlaboratory study 10 laboratories from 9 different countries registered for participation. See appendix 4 for the number of participants per country. In this report, the results of the 2019 proficiency test are presented and discussed. This report is also electronically available through the iis website www.iisnl.com.

2 SET UP

The Institute for Interlaboratory Studies (iis) in Spijkenisse, the Netherlands, was the organizer of this proficiency test (PT). Sample analyses for fit-for-use and homogeneity testing were subcontracted to an ISO/IEC17025 accredited laboratory. It was decided to send in this proficiency test one sample of Mouthwash (labelled #19645) and one sample of Toothpaste (labelled #19646), both were made positive (artificially fortified) with a number of heavy metals.
The participants were requested to report rounded and unrounded test results. The unrounded test results were preferably used for statistical evaluation.

2.1 QUALITY SYSTEM

The Institute for Interlaboratory Studies in Spijkenisse, the Netherlands, has implemented a quality system based on ISO/IEC17043:2010. This ensures strict adherence to protocols for sample preparation and statistical evaluation and 100% confidentiality of participant's data. Feedback from the participants on the reported data is encouraged and customer's satisfaction is measured on regular basis by sending out questionnaires.

2.2 PROTOCOL

The protocol followed in the organiszation of this proficiency test was the one as described for proficiency testing in the report 'iis Interlaboratory Studies: Protocol for the Organization, Statistics and Evaluation' of June 2018 (iis-protocol, version 3.5). This protocol is electronically available through the iis website www.iisnl.com, from the FAQ page.

2.3 CONFIDENTIALITY STATEMENT

All data presented in this report must be regarded as confidential and for use by the participating companies only. Disclosure of the information in this report is only allowed by means of the entire report. Use of the contents of this report for third parties is only allowed by written permission of the Institute for Interlaboratory Studies. Disclosure of the identity of one or more of the participating companies will be done only after receipt of a written agreement of the companies involved.

2.4 SAMPLES

A regular mouthwash was purchased from a local supermarket for the first batch and was artificially fortified with Cadmium, Lead and Mercury. From this batch 25 cups of 15 mL were filled with approximately 5 grams Mouthwash and labelled #19645. The homogeneity of the subsamples #19645 was checked by determination of Lead by using ICP-MS on five stratified randomly selected subsamples. See the following table for the test results.

	Lead as Pb in mg/kg
sample #19645-1	18.84
sample #19645-2	18.54
sample #19645-3	19.59
sample #19645-4	18.45
sample #19645-5	18.05

Table 2: homogeneity test results of subsamples #19645

From the above test results the repeatability was calculated and compared with 0.3 times the reproducibility of the reference method in agreement with the procedure of ISO13528, Annex B2, in the next table.

	Lead as Pb in mg/kg
r (observed)	1.61
reference method	Horwitz
0.3 * R (ref. method)	1.62

Table 3: evaluation of the repeatability of subsamples #19645

The calculated repeatability of sample #19645 is in agreement with 0.3 times the reproducibility of the reference method. Therefore, homogeneity of the subsamples was assumed.

A regular toothpaste was purchased from a local supermarket for the second batch and was artificially fortified with Cadmium, Lead and Mercury. From this batch 23 cups of 15 ml were filled with approximately 5 grams toothpaste and labelled #19646. The homogeneity of the subsamples #19646 was checked by determination of Cadmium and Lead by using ICP-MS on five stratified randomly selected subsamples. See the following table for the test results.

	Cadmium as Cd in mg/kg	Lead as Pb in mg/kg
sample #19646-1	5.46	17.22
sample #19646-2	5.23	17.12
sample #19646-3	5.42	18.04
sample #19646-4	5.38	17.36
sample #19646-5	5.34	17.61

Table 4: homogeneity test results of subsamples #19646

From the above test results the repeatabilities were calculated and compared with 0.3 times the reproducibility of the reference test method in agreement with the procedure of ISO13528, Annex B2, in the next table.

	Cadmium as Cd in mg/kg	Lead as Pb in mg/kg
r (observed)	0.25	1.03
reference method	Horwitz	Horwitz
0.3 * R (ref. method)	0.56	1.53

Table 5: evaluation of the repeatability of subsamples #19646

The calculated repeatability of sample #19646 is in agreement with 0.3 times the reproducibility of the reference method. Therefore, homogeneity of the subsamples was assumed.

To each of the participating laboratories one sample labelled #19645 (Mouthwash) and one sample labelled #19646 (Toothpaste) was sent on October 23, 2019. Due to leakage of mouthwash from the cup, vials of 8 mL were filled with 5 grams of mouthwash from the same homogeneous batch and sent to the participants on October 29, 2019.

2.5 ANALYSES

The participants were requested to determine on both samples the concentrations of Arsenic as As, Cadmium as Cd, Chromium as Cr, Lead as Pb, Mercury as Hg and Nickel as Ni, applying the analytical procedure that is routinely used in the laboratory. Also, some analytical details were asked.

It was explicitly requested to treat the samples as if they were routine samples and to report the test results using the indicated units on the report form and not to round the results, but report as much significant figures as possible. It was also requested not to report ‘less than’ results, which are above the detection limit, because such results cannot be used for meaningful statistical evaluations.

To get comparable results, a detailed report form and a letter of instructions are prepared. On the report form the reporting units are given as well as the appropriate reference test method that will be used during the evaluation. The detailed report form and the letter of instructions are both made available on the data entry portal www.kpmd.co.uk/sgs-iis-cts. The participating laboratories are also requested to confirm the sample receipt on this data entry portal. The letter of instructions can also be downloaded from the iis website www.iisnl.com.

3 RESULTS

During five weeks after sample dispatch, the test results of the individual laboratories were gathered via the data entry portal www.kpmd.co.uk/sgs-iis-cts/. The reported test results are tabulated per determination in appendix 1 and 2 of this report. The laboratories are presented by their code numbers.

Directly after the deadline, a reminder was sent to those laboratories that had not reported test results at that moment. Shortly after the deadline, the available test results were screened for suspect data. A test result was called suspect in case the Huber Elimination Rule (a robust outlier test) found it to be an outlier. The laboratories that produced these suspect data were asked to check the reported test results (no reanalysis). Additional or corrected test results are used for data analysis and original test results are placed under 'Remarks' in the test result tables in appendix 1. Test results that came in after the deadline were not taken into account in this screening for suspect data and thus these participants were not requested for checks.

3.1 STATISTICS

The protocol followed in the organization of this proficiency test was the one as described for proficiency testing in the report ‘iis Interlaboratory Studies: Protocol for the Organisation, Statistics and Evaluation’ of June 2018 (iis-protocol, version 3.5).
For the statistical evaluation, the *unrounded* (when available) figures were used instead of the rounded test results. Test results reported as ‘<…’ or ‘>…’ were not used in the statistical evaluation.

First, the normality of the distribution of the various data sets per determination was checked by means of the Lilliefors-test, a variant of the Kolmogorov-Smirnov test and by the calculation of skewness and kurtosis. Evaluation of the three normality indicators in combination with the visual evaluation of the graphic Kernel density plot, lead to judgement of the normality being either 'unknown', 'OK', 'suspect' or 'not OK'. After removal of outliers, this check was repeated. If a dataset does not have a normal distribution, the (results of the) statistical evaluation should be used with due care.

According to ISO5725 the original test results per determination were submitted to Dixon's, Grubbs' and/or Rosner's outlier tests. Outliers are marked by D(0.01) for the Dixon's test, by G(0.01) or DG(0.01) for the Grubbs' test and by R(0.01) for the Rosner's test. Stragglers are marked by D(0.05) for the Dixon's test, by G(0.05) or DG(0.05) for the Grubbs' test and by R(0.05) for the Rosner's test. Both outliers and stragglers were not included in the calculations of averages and standard deviations.

For each assigned value, the uncertainty was determined in accordance with ISO13528. Subsequently the calculated uncertainty was evaluated against the respective requirement based on the target reproducibility in accordance with ISO13528. In this PT, the criterion of ISO13528, paragraph 9.2.1 was met for all evaluated tests, therefore, the uncertainty of all assigned values may be negligible and need not be included in the PT.

Finally, the reproducibilities were calculated from the standard deviations by multiplying them with a factor of 2.8.

3.2 GRAPHICS

In order to visualize the data against the reproducibilities from literature, Gauss plots were made, using the sorted data for one determination (see appendix 1). On the Y-axis, the reported test results are plotted. The corresponding laboratory numbers are on the X-axis.

The straight horizontal line presents the consensus value (a trimmed mean). The four striped lines, parallel to the consensus value line, are the +3s, +2s, -2s and -3s target reproducibility limits of the selected reference test method. Outliers and other data, which were excluded from the calculations, are represented as a cross. Accepted data are represented as a triangle.
Furthermore, Kernel Density Graphs were made. This is a method for producing a smooth density approximation to a set of data that avoids some problems associated with histograms. Also, a normal Gauss curve was projected over the Kernel Density Graph for reference.

3.3 Z-SCORES

To evaluate the performance of the participating laboratories the z-scores were calculated. As it was decided to evaluate the performance of the participants in this proficiency test (PT) against the literature requirements, the z-scores were calculated using a target standard deviation. This results in an evaluation independent of the variation of this interlaboratory study.

The target standard deviation was calculated from the literature reproducibility by division with 2.8. In case no literature reproducibility was available, other target values were used. In some cases, a reproducibility based on former iis proficiency tests could be used.

When a laboratory did use a test method with a reproducibility that is significantly different from the reproducibility of the reference test method used in this report, it is strongly advised to recalculate the z-score, while using the reproducibility of the actual test method used, this in order to evaluate whether the reported test result is fit-for-use.

The z-scores were calculated according to:

$z_{(target)}$ = (test result - average of PT) / target standard deviation

The $z_{(target)}$ scores are listed in the test result tables in appendix 1.

Absolute values for z<2 are very common and absolute values for z>3 are very rare.
The usual interpretation of z-scores is as follows:

	$\lvert z\rvert < 1$	good
$1 <$	$\lvert z\rvert < 2$	satisfactory
$2 <$	$\lvert z\rvert < 3$	questionable
$3 <$	$\lvert z\rvert$	unsatisfactory

4 EVALUATION

During the execution of this proficiency test some problems occurred with the dispatch of the mouthwash sample. Some participants reported to have received a sample of Mouthwash which had leaked. Samples of mouthwash in 8 mL vials were sent to participants within a week of the dispatch date of this PT.

Two participants did not report any test results. The 8 participants reported 40 numerical test results. Observed was 1 outlying test results, which is 2.5% of the numerical test results. In proficiency studies, outlier percentages of 3% - 7.5% are quite normal.

Not all original data sets proved to have a normal Gaussian distribution. These are referred to as “not OK’, “suspect” or "unknown". The statistical evaluation of these data sets should be used with due care, see also paragraph 3.1.

4.1 EVALUATION PER SAMPLE AND PER ELEMENT

In this section, the results are discussed per sample and per element. The evaluation of the test results reported on the samples are summarised in appendix 1. The abbreviations, used in these tables, are explained in appendix 5.

Unfortunately, a suitable reference test method, providing the precision data, is not available for the determinations of heavy metals in personal care products, therefore the calculated reproducibilities were compared against the reproducibility estimated from the Horwitz equation.

Sample #19645, Mouthwash

Cadmium as Cd: This determination was not problematic. One statistical outlier was observed. However, the calculated reproducibility after rejection of the statistical outlier is in agreement with the estimated reproducibility using the Horwitz equation.

Lead as Pb: This determination was not problematic. No statistical outliers were observed. The calculated reproducibility is in full agreement with the estimated reproducibility using the Horwitz equation.

Mercury as Hg: This determination was not problematic. No statistical outliers were observed. The calculated reproducibility is in agreement with the estimated reproducibility using the Horwitz equation.

Other metals: The majority of participants agreed on a concentration near or below the limit of detection for Arsenic, Chromium and Nickel.

Sample #19646, Toothpaste

Cadmium as Cd: This determination was not problematic. No statistical outliers were observed. However, the calculated reproducibility is in agreement with the estimated reproducibility using the Horwitz equation.

Lead as Pb: This determination was not problematic. No statistical outliers were observed. The calculated reproducibility is in agreement with the estimated reproducibility using the Horwitz equation.

Mercury as Hg: This determination was not problematic. No statistical outliers were observed. The calculated reproducibility is in full agreement with the estimated reproducibility using the Horwitz equation.

Other metals: The majority of participants agreed on a concentration near or below the limit of detection for Arsenic, Chromium and Nickel.

4.2 PERFORMANCE EVALUATION FOR THE GROUP OF LABORATORIES

A comparison has been made between the reproducibilities as declared by the relevant reference method and the reproducibilities as found for the group of participating laboratories. The number of significant test results, the average result, the calculated reproducibility (2.8 * standard deviation) and the target reproducibility derived from the reference method (in casu Horwitz Equation) are presented in the next table.

Element	unit	n	average	2.8 * sd	R (target)
Cadmium as Cd	mg/kg	7	5.2	1.4	1.8
Lead as Pb	mg/kg	7	22.5	6.4	6.3
Mercury as Hg	mg/kg	5	2.4	0.7	1.0

Table 6: reproducibilities of tests on sample #19645

Element	unit	n	average	2.8 * sd	R (target)
Cadmium as Cd	mg/kg	8	6.6	1.5	2.2
Lead as Pb	mg/kg	7	23.9	5.8	6.6
Mercury as Hg	mg/kg	5	1.6	0.7	0.7

Table 7: reproducibilities of tests on sample #19646

From the table above, it can be concluded that, without statistical calculations, the group of participating laboratories do not have difficulties with the analysis of Metals in Mouthwash or Toothpaste when compared with the target reproducibility. See also paragraph 4.1.

4.3 UNCERTAINTIES OF THE PROFICIENCY TEST OF NOVEMBER 2019

The uncertainties observed in the test results of the determination of Trace Metals in Mouthwash and Toothpaste iis19H04 are listed in the next table.

Element	November 2019	Target (Horwitz)
Cadmium as Cd	8-9%	12% (at 5 mg/kg)
Lead as Pb	9-10%	10% (at 20 mg/kg)
Mercury as Hg	10-14%	14-16% (at 1-2 mg/kg)

Table 8: overview of uncertainties (RSD).

4.4 EVALUATION ANALYTICAL DETAILS

For this PT some analytical details were requested, see appendix 3. Based on the answers given by the participants the following can be summarized:
Six of the eight reporting participants mentioned that they are accredited for determination of Heavy Metals in Mouthwash and/or Toothpaste.
The other questions were about the intake of the sample used for the analyzes. Six of the eight reporting laboratories used between 0.2 – 0.5 gram, one participant used 1 gram and another used 10 grams.
Eight participants used ICP-MS to determine the metal content. One participant reported to use a different method to determine Mercury (AFS).

5 DISCUSSION AND CONCLUSION

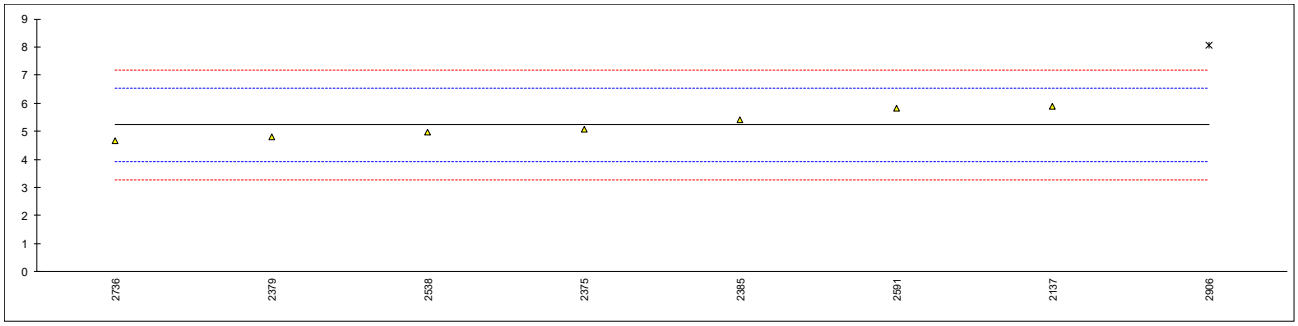
In this proficiency test the added metals in two different types of cosmetic products were correctly identified.

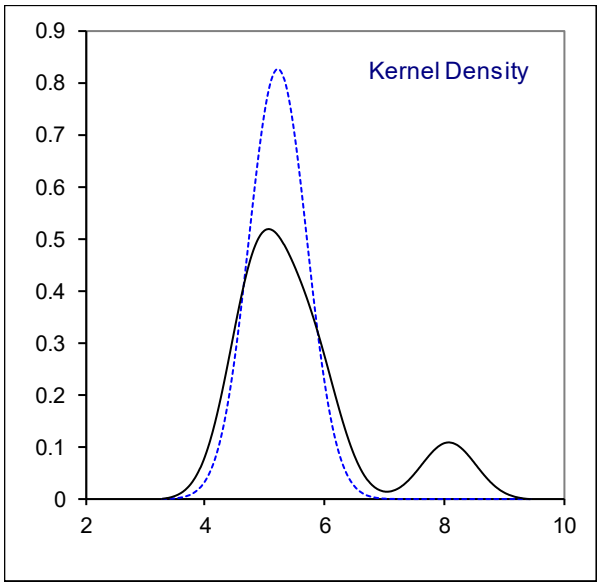
Each laboratory has to evaluate its performance in this study and make decisions about necessary corrective actions. Therefore, participation on a regular basis in this scheme could be helpful to improve the performance and thus increase of the quality of the analytical results.

APPENDIX 1

Determination of Cadmium as Cd in Mouthwash, sample #19645; results in mg/kg

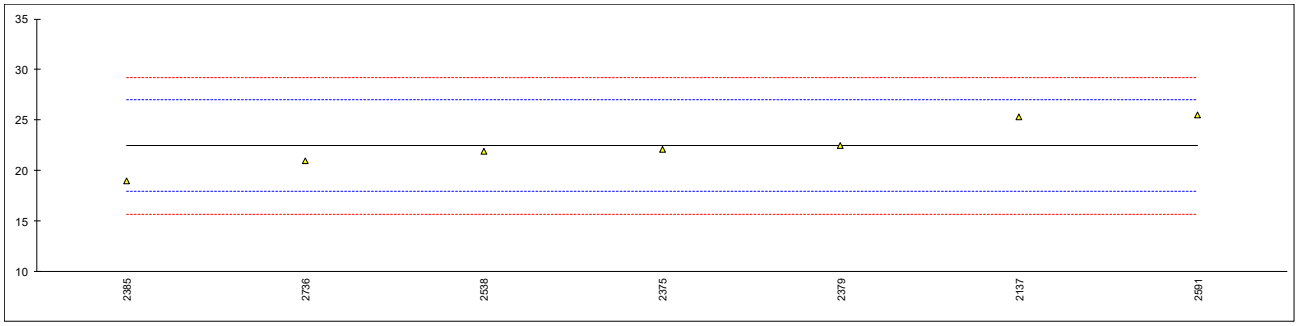
lab	method	value	mark	z(targ)	remarks
2137	MFDS Notification no.2019-93	5.9		1.02	
2375	In house	5.06		-0.26	
2379	In house	4.81		-0.65	
2385	In house	5.4		0.26	
2480		-----		-----	
2497		-----		-----	
2538		4.981		-0.38	
2591	In house	5.804		0.88	
2736	In house	4.665		-0.87	
2906	Safety and Technical Standard for Cosmetics (2015)	8.08	D(0.05)	4.37	
	normality	OK			
	n	7			
	outliers	1			
	mean (n)	5.231			
	st.dev. (n)	0.4820	RSD = 9%		
	R(calc.)	1.350			
	st.dev.(Horwitz)	0.6525			
	R(Horwitz)	1.827			

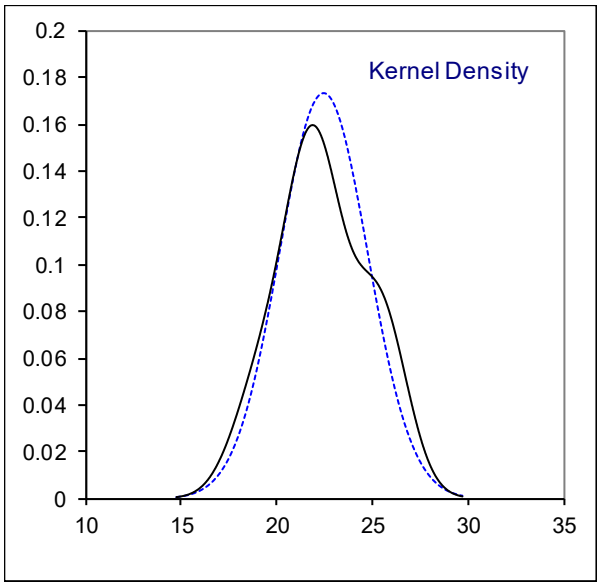




Determination of Lead as Pb in Mouthwash, sample #19645; results in mg/kg

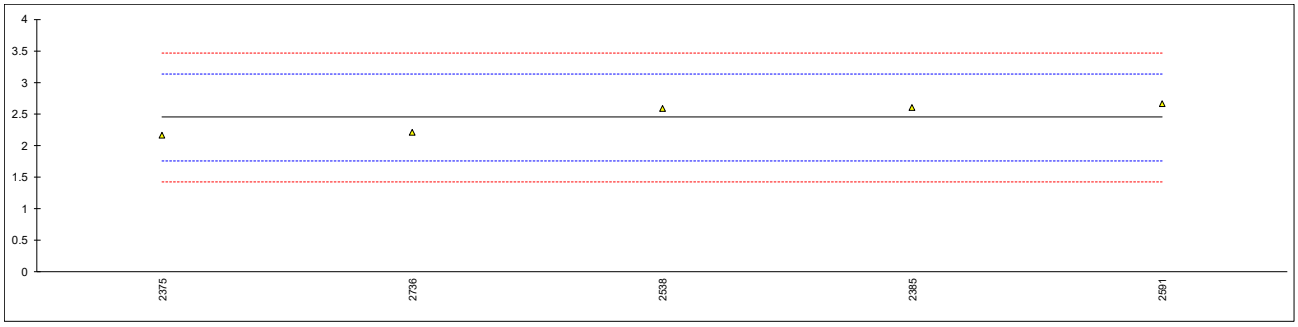
lab	method	value	mark	z(targ)	remarks
2137	MFDS Notification no.2019-93	25.3		1.26	
2375	In house	22.12	C	-0.16	
2379	In house	22.44		-0.01	
2385	In house	19		-1.54	
2480		-----		-----	
2497		-----		-----	
2538		21.95		-0.23	
2591	In house	25.504		1.35	
2736	In house	20.992		-0.66	
2906		-----		-----	
	normality	OK			
	n	7			
	outliers	0			
	mean (n)	22.472			
	st.dev. (n)	2.3034	RSD = 10%		
	R(calc.)	6.449			
	st.dev.(Horwitz)	2.2507			
	R(Horwitz)	6.302			





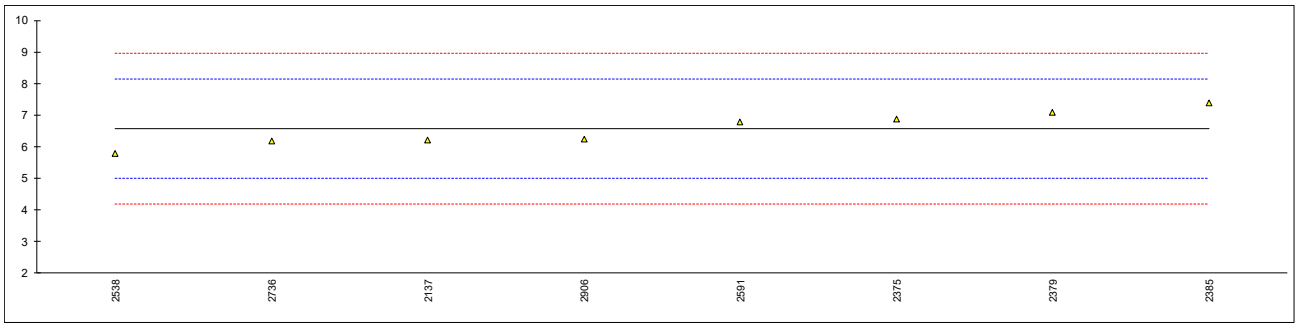
Determination of Mercury as Hg in Mouthwash, sample #19645; results in mg/kg

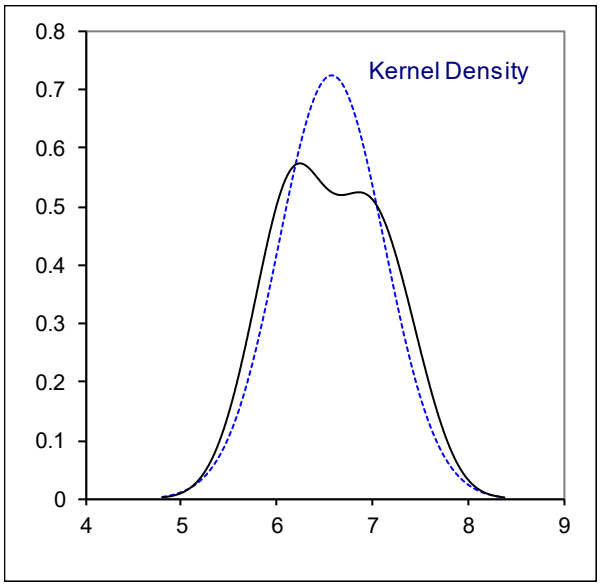
lab	method	value	mark	z(targ)	remarks
2137		-----		-----	
2375	In house	2.17		-0.80	
2379		-----		-----	
2385	In house	2.6		0.45	
2480		-----		-----	
2497		-----		-----	
2538		2.581		0.40	
2591	In house	2.668		0.65	
2736	In house	2.204		-0.70	
2906		-----		-----	
	normality	Unknown			
	n	5			
	outliers	0			
	mean (n)	2.445			
	st.dev. (n)	0.2377	RSD = 10%		
	R(calc.)	0.665			
	st.dev.(Horwitz)	0.3419			
	R(Horwitz)	0.957			



Determination of Cadmium as Cd in Toothpaste, sample #19646; results in mg/kg

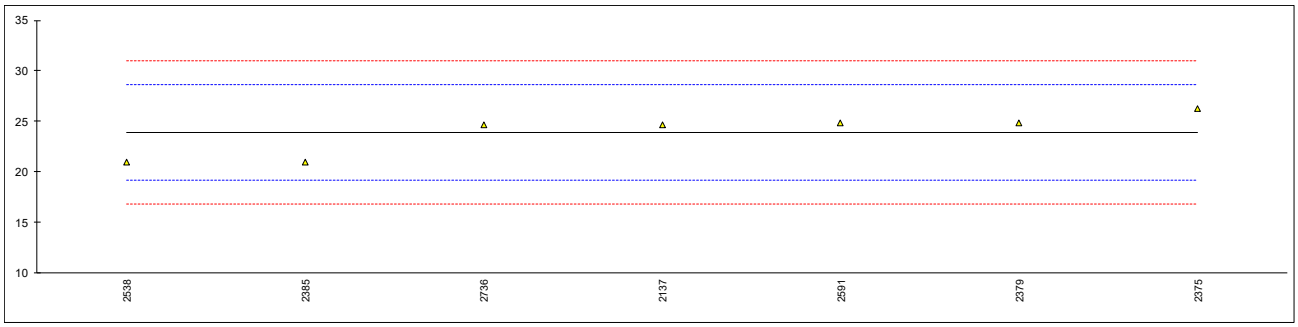
lab	method	value	mark	z(targ)	remarks
2137	MFDS Notification no. 23019-93	6.2		-0.47	
2375	In house	6.88		0.39	
2379	In house	7.09		0.65	
2385		7.4		1.05	
2480		-----		-----	
2497		-----		-----	
2538		5.779		-1.00	
2591	In house	6.795		0.28	
2736	In house	6.182		-0.49	
2906	Safety and Technical Standards for Cosmetics (2015)	6.25		-0.41	
	normality	OK			
	n	8			
	outliers	0			
	mean (n)	6.572			
	st.dev. (n)	0.5505	RSD = 8%		
	R(calc.)	1.541			
	st.dev.(Horwitz)	0.7920			
	R(Horwitz)	2.218			

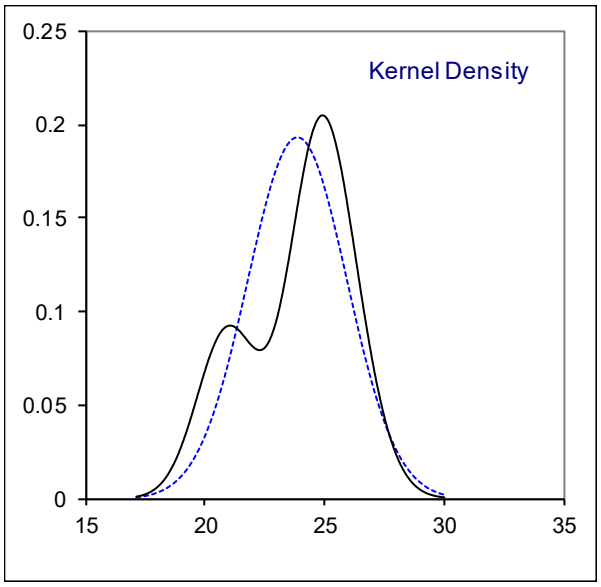




Determination of Lead as Pb in Toothpaste, sample #19646; results in mg/kg

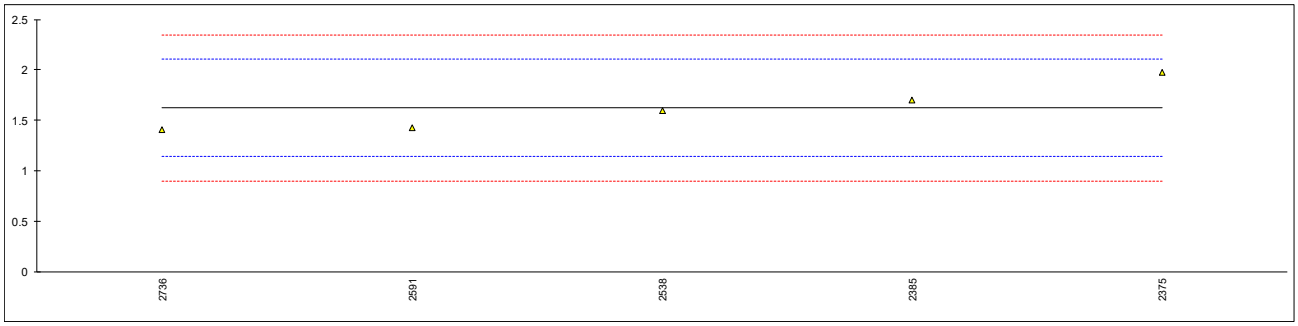
lab	method	value	mark	z(targ)	remarks
2137	MFDS Notification no. 23019-93	24.7		0.34	
2375	In house	26.25	C	1.00	
2379	In house	24.87		0.41	
2385		21		-1.22	
2480		-----		-----	
2497		-----		-----	
2538		20.94		-1.24	
2591	In house	24.856		0.41	
2736	In house	24.620		0.31	
2906		-----		-----	
	normality	OK			
	n	7			
	outliers	0			
	mean (n)	23.891			
	st.dev. (n)	2.0699	RSD = 9%		
	R(calc.)	5.796			
	st.dev.(Horwitz)	2.3709			
	R(Horwitz)	6.638			





Determination of Mercury as Hg in Toothpaste, sample #19646; results in mg/kg

lab	method	value	mark	z(targ)	remarks
2137		-----		-----	
2375	In house	1.98		1.48	
2379		-----		-----	
2385		1.7		0.32	
2480		-----		-----	
2497		-----		-----	
2538		1.602		-0.09	
2591	In house	1.425		-0.82	
2736	In house	1.411		-0.88	
2906		-----		-----	
	normality	unknown			
	n	5			
	outliers	0			
	mean (n)	1.624			
	st.dev. (n)	0.2334	RSD = 14%		
	R(calc.)	0.654			
	st.dev.(Horwitz)	0.2415			
	R(Horwitz)	0.676			



APPENDIX 2

Other reported Metals in sample #19645 (in mg/kg)

lab	As	Cr	Ni
2137	-----	-----	-----
2375	<0.083	<0.83	<0.83
2379	-----	-----	-----
2385	<0.5	<0.5	<0.5
2480	-----	-----	-----
2497	-----	-----	-----
2538	< 1.00	< 4.00	< 1.00
2591	<1.0	<1.0	<1.0
2736	<0.025	0.028	<0.025
2906	-----	-----	-----

Other reported Metals in sample #19646 (in mg/kg)

lab	As	Cr	Ni
2137	-----	-----	9.3
2375	<0.12	<0.83	<0.83
2379	0.15	-----	-----
2385	<0.5	<0.5	<0.5
2480	-----	-----	-----
2497	-----	-----	-----
2538	< 1.00	< 4.00	< 1.00
2591	<1.0	<1.0	<1.0
2736	0.196	0.394	0.234
2906	-----	-----	-----

APPENDIX 3

Analytical details

lab	ISO17025 accredited	Intake in gram	Technique used	remarks
2137	Yes	0.2	ICP-MS	
2375	Yes	10 grams	ICP-MS	
2379	Yes	0.25 gram	ICP-MS	
2385	Yes	Mouthwash 0.15-0.35g / Toothpaste 0.15-0.85g	ICP-MS	Double measurement
2480	---		---	
2497	---		---	
2538	Yes	0.25	ICP-OES, Hg: AFS	
2591	No	0.2 grams	ICP-MS	
2736	No	1 for mouthwash, 0.5 for toothpaste	ICP-MS	
2906	Yes	0.5544	ICP-MS	

APPENDIX 4

Number of participants per country

1 lab in FRANCE
2 labs in GERMANY
1 lab in ITALY
1 lab in P.R. of CHINA
1 lab in SOUTH KOREA
1 lab in SPAIN
1 lab in THAILAND
1 lab in TURKEY
1 lab in U.S.A.

APPENDIX 5

Abbreviations

C = final test result after checking of first reported suspect test result
D(0.01) = outlier in Dixon's outlier test
D(0.05) = straggler in Dixon's outlier test
G(0.01) = outlier in Grubbs' outlier test
G(0.05) = straggler in Grubbs' outlier test
DG(0.01) = outlier in Double Grubbs' outlier test
DG(0.05) = straggler in Double Grubbs' outlier test
R(0.01) = outlier in Rosner's outlier test
R(0.05) = straggler in Rosner's outlier test
ex = test result excluded from statistical evaluation
n.a. = not applicable
n.e. = not evaluated
n.d. = not detected

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