Statistical Methods in PQRI Interlaboratory Study Report

4th PQRI Workshop on ICH Q3D Elemental Impurities Requirements

Stephen W. Erickson, PhD

PQRI Interlaboratory Study on the Determination of Elemental Impurities in Drug Products

FINAL REPORT

Client: Product Quality Research Institute (PQRI)

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By

James M. Harrington, Ph.D.
RTI International
3040 Cornwallis Road
Research Triangle Park, NC 27709
jharrington@rti.org

Donna S. Seibert, Ph.D.
Perrigo Company
655 Hooker Road
Allegan, MI 49010
donna.seibert@perrigo.com

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Inter-laboratory validation of bioaccessibility testing for metals

Rayetta G. Henderson [a,*], Violaine Verougstraete [b], Kim Anderson [c], José J. Arbildua [d], Thomas O. Brock [e], Tony Brouwers [f], Danielle Cappellini [g], Katrien Delbeke [h], Gunilla Herting [i], Greg Hixon [a], Inger Odnevall Wallinder [i], Patricio H. Rodriguez [d], Frank Van Assche [j], Peter Wilrich [k], Adriana R. Oller [l]

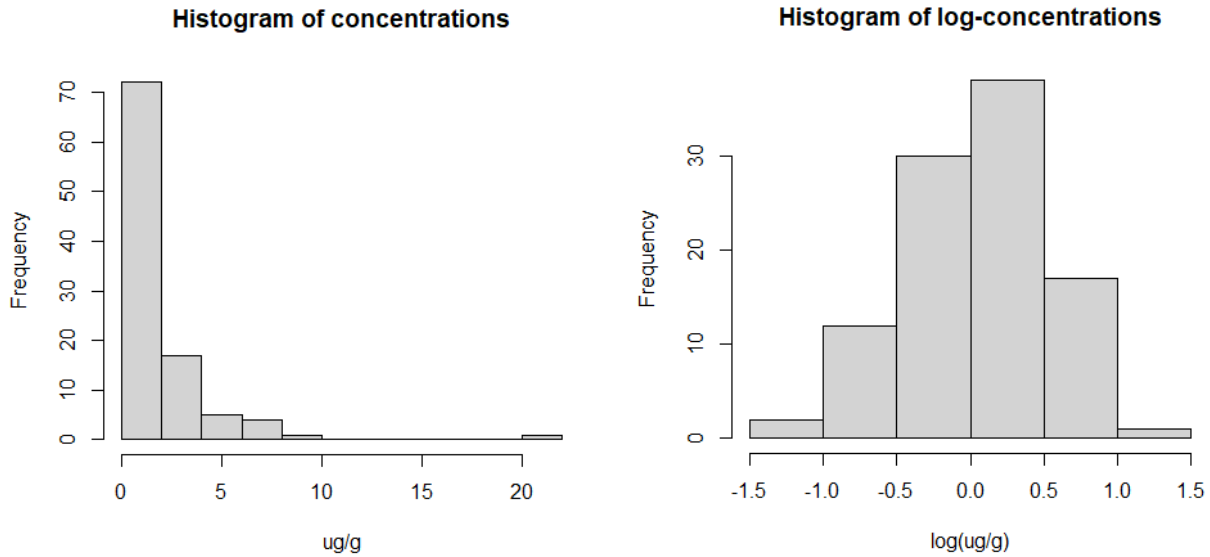
[a] ToxStrategies, Inc., 9650 Strickland Rd., Suite 103-195, Raleigh, NC 27615, USA
[b] Eurometaux, Avenue de Broqueville 12, 1150 Brussels, Belgium
[c] Oregon State University, Corvallis, OR 97331, USA
[d] CECM, Adolfo Ibañez University, Diagonal Las Torres 2640, Peñalolen, Santiago, Chile
[e] Duke University, 2200 West Main Street, Suite 400, Durham, NC 27705, USA
[f] ECTX bvba, Havenstraat 46/0.01, B-3500 Hasselt, Belgium
[g] Kirby Memorial Health Center, 71 North Franklin Street, Wilkes-Barre, PA 18701, USA
[h] European Copper Institute, 168 Avenue de Tervueren, 1150 Brussels, Belgium
[i] KTH Royal Institute of Technology, Drottning Kristinas väg 51, SE-10044 Stockholm, Sweden
[j] International Zinc Association, Avenue de Tervueren 168/Box 4, B-1150, Belgium
[k] Freie Universität Berlin, Promenadenstr. 16 A, D-12207 Berlin, Germany
[l] Nickel Producers Environmental Research Association, Inc., 2525 Meridian Parkway, Suite 240, Durham, NC 27713, USA

Appendices to be Discussed

- Appendix E: Comparison of ICP-MS results to Reference Values
- Appendix F: Analysis of Reproducibility of Analytical Results (ICP-MS)
- Appendix G: Comparison of Digestion Methods (EE vs TG)
- Appendix H: Comparison of Microwave systems (IPV vs SRC)
- Appendix I: Summation Approach Analysis
- Appendix J: Analysis of Analytical Results (XRF)

Preliminaries

- Means, standard deviations, confidence intervals, etc, were computed using log-transformed concentrations due to right-skewness



- For display purposes, these values were transformed back to the original units (*µg/g*)

Preliminaries

- Values below the limit of quantitation were including in mean calculations, set equal to the limit of quantitation
- Standard deviations were calculated only using values that were greater than the limit of quantitation
- *t*-tests and *F*-tests were used to compare means and variances, respectively

Table E1. Comparison of ICP-MS values to Reference Values

Analyte	Material	Method	Total Measurements (n)	Measurements >LOQ (n)	Reference concentration (ug/g)	Mean concentration (ug/g)	Geometric standard deviation (ug/g)	95% confidence Interval	P value
As	Lactose	Exhaustive	42	3	ND	0.2	4.1	(0.0, 0.8)	NA
		Total	18	0	ND	ND	NA	NA	NA
		All labs	60	3	ND	0.2	4.1	(0.0, 0.8)	NA
	Magnesium Aluminum Silicate	Exhaustive	42	15	1.74	7.4	8.4	(2.5, 21.7)	0.020
		Total	18	0	1.90	ND	NA	NA	NA
		All labs	60	15	1.79	7.4	8.4	(2.5, 21.7)	0.022
	Red Ferric Oxide	Exhaustive	42	5	0.442	1.1	3.8	(0.3, 3.5)	0.215
		Total	18	3	0.473	40	1	(40, 40)	NA
		All labs	60	8	0.451	4.2	8.4	(1.0, 18.2)	0.021
	Silicon Dioxide Standard (As, Co, Hg)	Exhaustive	41	41	1090	998	1	(949, 1050)	0.001
		Total	17	15	988	1007	1	(969, 1047)	0.337
		All labs	58	56	1060	1001	1	(963, 1040)	0.005
	Silicon Dioxide Standard (Cd, Ni, Pb)	Exhaustive	39	4	ND	2.3	1.2	(1.8, 2.8)	NA
		Total	18	0	ND	ND	NA	NA	NA
		All labs	57	4	ND	2.3	1.2	(1.8, 2.8)	NA
	Starch	Exhaustive	42	3	ND	0.6	1.4	(0.4, 1.0)	NA
		Total	18	0	ND	ND	NA	NA	NA
		All labs	60	3	ND	0.6	1.4	(0.4, 1.0)	NA
	Tablet Level 1	Exhaustive	57	57	5.65	6.1	1.5	(5.5, 6.8)	0.157
		Total	21	21	6.05	5.5	1.2	(5.1, 5.9)	0.015
		All labs	78	78	5.76	5.9	1.4	(5.5, 6.4)	0.485
	Tablet Level 2	Exhaustive	57	57	17.0	17	1	(16, 18)	0.530
		Total	21	21	17.9	17	1	(17, 18)	0.004
		All labs	78	78	17.2	17	1	(16, 17)	0.242

Table E1. Comparison of ICP-MS values to Reference Values

Analyte	Material	Method	Total Measurements (n)	Measurements >LOQ (n)	Reference concentration (ug/g)	Mean concentration (ug/g)	Geometric standard deviation (ug/g)	95% confidenc Interval	P value
As	Lactose	Exhaustive	42	3	ND	0.2	4.1	(0.0, 0.8)	NA
		Total	18	0	ND	ND	NA	NA	NA
		All labs	60	3	ND	0.2	4.1	(0.0, 0.8)	NA
	Magnesium Aluminum Silicate	Exhaustive	42	15	1.74	7.4	8.4	(2.5, 21.7)	0.020
		Total	18	0	1.90	ND	NA	NA	NA
		All labs	60	15	1.79	7.4	8.4	(2.5, 21.7)	0.022
	Red Ferric Oxide	Exhaustive	42	5	0.442	1.1	3.8	(0.3, 3.5)	0.215
		Total	18	3	0.473	40	1	(40, 40)	NA
		All labs	60	8	0.451	4.2	8.4	(1.0, 18.2)	0.021
	Silicon Dioxide Standard (As, Co, Hg)	Exhaustive	41	41	1090	998	1	(949, 1050)	0.001
		Total	17	15	988	1007	1	(969, 1047)	0.337
		All labs	58	56	1060	1001	1	(963, 1040)	0.005
	Silicon Dioxide Standard (Cd, Ni, Pb)	Exhaustive	39	4	ND	2.3	1.2	(1.8, 2.8)	NA
		Total	18	0	ND	ND	NA	NA	NA
		All labs	57	4	ND	2.3	1.2	(1.8, 2.8)	NA
	[illegible]	Exhaustive	42	3	ND	0.6	1.4	(0.4, 1.0)	NA
		Total	18	0	ND	ND	NA	NA	NA
		All labs	60	3	ND	0.6	1.4	(0.4, 1.0)	NA
	Tablet Level 1	Exhaustive	57	57	5.65	6.1	1.5	(5.5, 6.8)	0.157
		Total	21	21	6.05	5.5	1.2	(5.1, 5.9)	0.015
		All labs	78	78	5.76	5.9	1.4	(5.5, 6.4)	0.485
	Tablet Level 2	Exhaustive	57	57	17.0	17	1	(16, 18)	0.530
		Total	21	21	17.9	17	1	(17, 18)	0.004
		All labs	78	78	17.2	17	1	(16, 17)	0.242

One-sample t-test, mean ICP-MS vs reference

Repeatability vs Reproducibility

- Repeatability standard deviation (S_r) indicates the variability of measurements within labs
- Reproducibility standard deviation (S_R) indicates the variability of measurements between labs
- These are computed with analysis of variance (ANOVA)
- The ratio S_R:S_r indicates the relative agreement of results between labs
- S_R:S_r < 6 is considered “good” agreement between labs

Table F1. Reproducibility Results for ICP-MS Results Arranged by Analyte

Analyte	Material	Labs (n)	Measurements reported (n)	Measurements >LOQ (n)	Mean concentration (µg/g)	Within Lab Standard deviation (s_r, µg/g)	Within lab Geometric CV	Between Lab Standard deviation (s_R, µg/g)	Between lab Geometric CV	S_R:S_r ratio
As	Lactose	16	69	3	0.2	4.1	250%	NA	NA	NA
	Magnesium Aluminum Silicate	16	69	21	5.1	1.3	26%	30.5	>300%	13.6
	Microcrystalline Cellulose	16	69	8	4.2	1.3	31%	25.9	>300%	10.9
	Red Ferric Oxide	16	69	14	1.1	6.1	5.1%	30.9	>300%	1.89
	Silicon Dioxide Standard (As, Co, Hg)	16	65	63	1000	1	6.1%	1	26%	4.20
	Silicon Dioxide Standard (Cd, Ni, Pb)	15	66	6	1.3	1.5	40%	4.3	272%	3.79
	Standard Liquid[a]	18	38	35	4.2	1.1	5.0%	1.8	63%	11.6
	Starch	16	69	4	0.3	1.4	38%	8.5	>300%	5.87
	Stearic Acid	14	57	3	0.3	1.9	73%	NA	NA	NA
	Tablet Level 1	22	87	87	5.9	1.2	14%	1.9	70%	4.40
	Tablet Level 2	22	87	87	17	1	12%	1	24%	1.96
	Tablet Level 3	22	87	87	42	1	7.6%	1	40%	5.03
Cd	Lactose	16	69	2	0.05	12.5	>300%	NA	NA	NA
	Magnesium Aluminum Silicate	16	69	15	0.2	1.7	57%	99.5	>300%	8.68
	Microcrystalline Cellulose	16	69	7	0.9	1.6	48%	73.6	>300%	9.45
	Red Ferric Oxide	16	69	7	0.10	1.20	19%	508.25	>300%	33.2
	Silicon Dioxide Standard (As, Co, Hg)	15	62	17	8.0	2.0	80%	5059.0	>300%	12.2
	Silicon Dioxide Standard (Cd, Ni, Pb)	16	69	69	952	1	13%	1	21%	1.56

Table F1. Reproducibility Results for ICP-MS Results Arranged by Analyte

Analyte	Material	Labs (n)	Measurements reported (n)	Measurements >LOQ (n)	Mean concentration (µg/g)	Within Lab Standard deviation (s_r, µg/g)	Within lab Geometric CV	Between Lab Standard deviation (s_R, µg/g)	Between lab Geometric CV	S_R:S_r ratio
As	Lactose	16	69	3	0.2	4.1	250%	NA	NA	NA
	Magnesium Aluminum Silicate	16	69	21	5.1	1.3	26%	30.5	>300%	24.1
	Microcrystalline Cellulose	16	69	8	4.2	1.3	31%	25.9	>300%	10.9
	Red Ferric Oxide	16	69	14	1.1	6.1	5.1%	30.9	>300%	1.89
	Silicon Dioxide Standard (As, Co, Hg)	16	65	63	1000	1	6.1%	1	26%	4.20
	Silicon Dioxide Standard (Cd, Ni, Pb)	15	66	6	1.3	1.5	40%	4.3	272%	3.79
	Standard Liquid[a]	18	38	35	4.2	1.1	5.0%	1.8	63%	11.6
	Starch	16	69	4	0.3	1.4	38%	8.5	>300%	5.87
	Stearic Acid	14	57	3	0.3	1.9	73%	NA	NA	NA
	Tablet Level 1	22	87	87	5.9	1.2	14%	1.9	70%	4.40
	Tablet Level 2	22	87	87	17	1	12%	1	24%	1.96
	Tablet Level 3	22	87	87	42	1	7.6%	1	40%	5.03
Cd	Lactose	16	69	2	0.05	12.5	>300%	NA	NA	NA
	Magnesium Aluminum Silicate	16	69	15	0.2	1.7	57%	99.5	>300%	8.68
	Microcrystalline Cellulose	16	69	7	0.9	1.6	48%	73.6	>300%	9.45
	Red Ferric Oxide	16	69	7	0.10	1.20	19%	508.25	>300%	33.2
	Silicon Dioxide Standard (As, Co, Hg)	15	62	17	8.0	2.0	80%	5059.0	>300%	12.2
	Silicon Dioxide Standard (Cd, Ni, Pb)	16	69	69	952	1	13%	1	21%	1.56

Calculated from log-concentrations!

Appendix G: Comparison of Digestion Methods (EE vs TG)

Analyte	Material	Method	Labs (n)	Measurements Reported (n)	Measurements >LOQ (n)	Mean concentration (ug/g)	P value	Within lab standard deviation (ug/g)	P value	Between lab standard deviation (ug/g)	P value
As	Lactose	Exhaustive	13	42	3	0.158	NA	NA	NA	NA	NA
		Total	6	18	0	ND		NA		NA	
	Magnesium Aluminum Silicate	Exhaustive	13	42	15	7.4	NA	1.3	NA	52.3	NA
		Total	6	18	0	ND		NA		NA	
	Microcrystalline Cellulose	Exhaustive	13	42	8	4.2	NA	1.3	NA	25.9	NA
		Total	6	18	0	ND		NA		NA	
	Red Ferric Oxide	Exhaustive	13	42	5	1.1	0.004	1.1	NA	14.7	NA
		Total	6	18	3	40		NA		NA	
	Silicon Dioxide Standard (As, Co, Hg)	Exhaustive	13	41	41	998	0.776	1	0.056	1	0.142
		Total	6	17	15	1010		0		0	
	Silicon Dioxide Standard (As, Co, Hg)	Exhaustive	12	39	4	2.3	NA	1.3	NA	1.2	NA
		Total	6	18	0	ND		NA		NA	
	Starch	Exhaustive	13	42	3	0.648	NA	NA	NA	NA	NA
		Total	6	18	0	ND		NA		NA	
	Stearic Acid	Exhaustive	11	36	3	0.332	NA	NA	NA	NA	NA
		Total	4	12	0	ND		NA		NA	
	Tablet Level 1	Exhaustive	19	57	57	6.1	0.098	1.2	0.001	1.9	0.06
		Total	7	21	21	5.5		1.1		1.4	
	Tablet Level 2	Exhaustive	19	57	57	17	0.308	1	< 0.001	1	0.018
		Total	7	21	21	17		1		1	
	Tablet Level 3	Exhaustive	19	57	57	41	0.03	1	< 0.001	2	0.004
		Total	7	21	21	44		1		1	
Cd	Lactose	Exhaustive	13	42	2	0.048	NA	NA	NA	NA	NA
		Total	6	18	0	ND		NA		NA	
	Magnesium Aluminum Silicate	Exhaustive	13	42	9	0.4	NA	2.0	NA	244.1	NA
		Total	6	18	0	ND		NA		NA	
		Exhaustive	13	42	7	0.9	NA	1.6	NA	73.6	NA

P-values compare methods (F-test)

Analyte	Material	Method	Labs (n)	Measurements Reported (n)	Measurements >LOQ (n)	Mean concentration (ug/g)	P value	Within lab standard deviation (ug/g)	P value	Between lab standard deviation (ug/g)	P value
As	Lactose	Exhaustive	13	42	3	0.158	NA	NA	NA	NA	NA
		Total	6	18	0	ND		NA		NA	
	Magnesium Aluminum Silicate	Exhaustive	13	42	15	7.4	NA	1.3	NA	52.3	NA
		Total	6	18	0	ND		NA		NA	
	Microcrystalline Cellulose	Exhaustive	13	42	8	4.2	NA	1.3	NA	25.9	NA
		Total	6	18	0	ND		NA		NA	
	Red Ferric Oxide	Exhaustive	13	42	5	1.1	0.004	1.1	NA	14.7	NA
		Total	6	18	3	40		NA		NA	
	Silicon Dioxide Standard (As, Co, Hg)	Exhaustive	13	41	41	998	0.776	1	0.056	1	0.142
		Total	6	17	15	1010		0		0	
	Silicon Dioxide Standard (As, Co, Hg)	Exhaustive	12	39	4	2.3	NA	1.3	NA	1.2	NA
		Total	6	18	0	ND		NA		NA	
	Starch	Exhaustive	13	42	3	0.648	NA	NA	NA	NA	NA
		Total	6	18	0	ND		NA		NA	
	Stearic Acid	Exhaustive	11	36	3	0.332	NA	NA	NA	NA	NA
		Total	4	12	0	ND		NA		NA	
	Tablet Level 1	Exhaustive	19	57	57	6.1	0.098	1.2	0.001	1.9	0.06
		Total	7	21	21	5.5		1.1		1.4	
	Tablet Level 2	Exhaustive	19	57	57	17	0.308	1	< 0.001	1	0.018
		Total	7	21	21	17		1		1	
	Tablet Level 3	Exhaustive	19	57	57	41	0.03	1	< 0.001	2	0.004
		Total	7	21	21	44		1		1	
Cd	Lactose	Exhaustive	13	42	2	0.048	NA	NA	NA	NA	NA
		Total	6	18	0	ND		NA		NA	
	Magnesium Aluminum Silicate	Exhaustive	13	42	9	0.4	NA	2.0	NA	244.1	NA
		Total	6	18	0	ND		NA		NA	
		Exhaustive	13	42	7	0.9	NA	1.6	NA	73.6	NA

Appendix H: Comparison of Microwave systems (IPV vs SRC)

Analyte	Material	Microwave Type	Labs (n)	Total Measurements (n)	Measurements >LOQ (n)	Mean concentration (ug/g)	P value	Within lab standard deviation (ug/g)	P value	Between lab standard deviation (ug/g)	P value
As	Lactose	IPV	4	15	0	ND	NA	NA	NA	NA	NA
		SRC	12	54	3	0.158		NA		NA	
	Magnesium Aluminum Silicate	IPV	4	15	6	33	0.07	2	< 0.001	489	0.002
		SRC	12	54	15	2.4		1.1		2.1	
	Microcrystalline Cellulose	IPV	4	15	3	52	0.007	NA	NA	NA	NA
		SRC	12	54	5	0.9		1.7		7.3	
	Red Ferric Oxide	IPV	4	15	2	0.246	0.029	NA	NA	NA	NA
		SRC	12	54	12	1.4		6.8		48.4	
	Silicon Dioxide Standard (As, Co, Hg)	IPV	4	15	15	1032	0.171	1	0.98	1	0.189
		SRC	12	50	48	991		1		1	
	Silicon Dioxide Standard (As, Co, Hg)	IPV	4	15	1	2.0	NA	NA	NA	NA	NA
		SRC	11	51	5	1.1		1.5		7.4	
	Standard Liquid	IPV	6	14	14	3.6	0.049	1.1	0.002	1.5	0.308
		SRC	12	24	21	4.6		1.0		1.9	
	Starch	IPV	4	15	0	ND	NA	NA	NA	NA	NA
		SRC	12	54	4	0.3		1.4		8.5	
	Stearic Acid	IPV	4	15	0	ND	NA	NA	NA	NA	NA
		SRC	10	42	3	0.332		NA		NA	
	Tablet Level 1	IPV	8	27	27	6.7	0.1	1.3	< 0.001	2.5	0.009
		SRC	14	60	60	5.6		1.1		1.5	
	Tablet Level 2	IPV	8	27	27	17	0.361	1	0.018	1	0.24
		SRC	14	60	60	17		1		1	
	Tablet Level 3	IPV	8	27	27	41	0.54	1	< 0.001	2	0.004
		SRC	14	60	60	43		1		1	
Cd	Lactose	IPV	4	15	0	ND	NA	NA	NA	NA	NA
		SRC	12	54	2	0.048		NA		NA	
		IPV	4	15	3	21	0.085	1	0.073	95	0.013

Table I1. Comparison of Direct analysis of tablets with summation approach for all labs

Analyte	Material	Quantitation Approach	Number of labs	Total Measurements (n)	Measurements >LOD (n)	Mean concentration (ug/g)	P value	Within lab standard deviation (ug/g)	P value	Between lab standard deviation (ug/g)	P value
As	Tablet Level 1	Standard	13	50	50	5.9	0.208	1.2	0.322	2.2	0.616
		Summation	13	50	50	6.6		1.2		2.6	
	Tablet Level 2	Standard	13	50	50	16	0.188	1	< 0.001	1	< 0.001
		Summation	13	50	50	18		1		3	
	Tablet Level 3	Standard	13	50	50	41	0.001	1	0.648	2	0.45
		Summation	13	50	48	48		1		1	
Cd	Tablet Level 1	Standard	13	50	50	1.9	0.663	1.4	0.028	1.3	< 0.001
		Summation	13	50	50	1.9		1.2		3.7	
	Tablet Level 2	Standard	13	50	47	4.4	0.001	1.1	0.015	1.3	< 0.001
		Summation	13	50	50	6.2		1.2		3.3	
	Tablet Level 3	Standard	13	50	48	13	0.002	1	< 0.001	2	0.197
		Summation	13	50	50	18		1		3	
Co	Tablet Level 1	Standard	13	50	50	8.6	0.783	1.2	0.03	1.4	0.006
		Summation	13	50	50	8.4		1.2		2.3	
	Tablet Level 2	Standard	13	50	47	18	0.843	1	0.756	1	< 0.001
		Summation	13	50	50	18		1		3	
	Tablet Level 3	Standard	13	50	48	38	0.269	1	< 0.001	2	< 0.001
		Summation	13	50	50	33		1		5	
Hg	Tablet Level 1	Standard	12	44	10	0.9	< 0.001	1.2	0.003	1.6	0.047
		Summation	12	44	38	6.0		1.1		1.2	
	Tablet Level 2	Standard	12	44	33	1.3	< 0.001	1.1	0.138	1.2	0.967
		Summation	12	44	38	18		1		1	
	Tablet Level 3	Standard	12	44	41	2.0	< 0.001	1.2	0.003	1.7	0.002
		Summation	12	44	38	45		1		1	
Ni	Tablet Level 1	Standard	13	50	50	8.7	0.717	1.2	0.184	1.4	0.058
		Summation	13	50	50	8.5		1.2		1.7	
	Tablet Level 2	Standard	13	50	50	9.9	0.128	1.8	< 0.001	2.9	0.108
		Summation	13	50	50	12		1		2	

Table I1. Comparison of Direct analysis of tablets with summation approach for all labs

Analyte	Material	Quantitation Approach	Number of labs	Total Measurements (n)	Measurements >LOD (n)	Mean concentration (ug/g)	P value	Within lab standard deviation (ug/g)	P value	Between lab standard deviation (ug/g)	P value
As	Tablet Level 1	Standard	13	50	50	5.9	0.208	1.2	0.322	2.2	0.616
		Summation	13	50	50	6.6		1.2		2.6	
	Tablet Level 2	Standard	13	50	50	[illegible]		1	< 0.001	1	< 0.001
		Summation	13	50	50	18		1		3	
	Tablet Level 3	Standard	13	50	50	41	0.001	1	0.648	2	0.45
		Summation	13	50	48	48		1		1	
Cd	Tablet Level 1	Standard	13	50	50	1.9	0.663	1.4	0.028	1.3	< 0.001
		Summation	13	50	50	1.9		1.2		3.7	
	Tablet Level 2	Standard	13	50	47	4.4	0.001	1.1	0.015	1.3	< 0.001
		Summation	13	50	50	6.2		1.2		3.3	
	Tablet Level 3	Standard	13	50	48	13	0.002	1	< 0.001	2	0.197
		Summation	13	50	50	18		1		3	
Co	Tablet Level 1	Standard	13	50	50	8.6	0.783	1.2	0.03	1.4	0.006
		Summation	13	50	50	8.4		1.2		2.3	
	Tablet Level 2	Standard	13	50	47	18	0.843	1	0.756	[illegible]	[illegible]
		Summation	13	50	50	18		1		3	
	Tablet Level 3	Standard	13	50	48	38	0.269	1	< 0.001	2	< 0.001
		Summation	13	50	50	33		1		5	
Hg	Tablet Level 1	Standard	12	44	10	0.9	< 0.001	1.2	0.003	1.6	0.047
		Summation	12	44	38	6.0		1.1		1.2	
	Tablet Level 2	Standard	12	44	33	1.3	< 0.001	1.1	0.138	1.2	0.967
		Summation	12	44	38	18		1		1	
	Tablet Level 3	Standard	12	44	41	2.0	< 0.001	1.2	0.003	1.7	0.002
		Summation	12	44	38	45		[illegible]		1	
Ni	Tablet Level 1	Standard	13	50	50	8.7	0.717	1.2	0.184	1.4	0.058
		Summation	13	50	50	8.5		1.2		1.7	
	Tablet Level 2	Standard	13	50	50	9.9	0.128	[illegible]	[illegible]	2.9	0.108
		Summation	13	50	50	12		1		2	

Table J1. Comparison of XRF values to Reference values

Analyte	Material	Total Measurements (n)	Measurements >LOQ (n)	Reference concentration (ug/g)	Mean concentration (ug/g)	Geometric standard dev (ug/g)	95% CI	P value	Expected concentration (µg/g)	% of expected value
As	Tablet Level 1	9	9	6.05	5.6	1.0	(5.5, 5.7)	< 0.001	6.65	84.7
	Tablet Level 2	9	9	17.9	19	1	(18, 19)	0.078	19.8	93.8
	Tablet Level 3	9	9	43.6	48	1	(47, 50)	< 0.001	49.2	98.5
Cd	Tablet Level 1	9	9	1.97	2.5	1.2	(2.2, 2.9)	0.007	1.58	160.9
	Tablet Level 2	9	9	4.61	7.2	1.3	(6.1, 8.5)	< 0.001	5.26	136.1
	Tablet Level 3	9	9	13.5	18	1	(15, 22)	0.019	15.755	113.9
Co	Tablet Level 1	9	9	9.02	8.1	1.7	(5.8, 11.4)	0.568	8.68	93.7
	Tablet Level 2	9	9	20.3	22	1	(18, 27)	0.545	22.08	98.5
	Tablet Level 3	9	9	40.4	41	1	(38, 45)	0.534	50.12	82.7
Hg	Tablet Level 1	7	4	3.80	2.6	1.2	(2.2, 3.1)	0.026	6.48	40.0
	Tablet Level 2	7	4	14.2	3.4	1.2	(2.8, 4.2)	< 0.001	19.45	17.6
	Tablet Level 3	7	7	41.2	3.6	2.2	(2.1, 6.4)	< 0.001	48.609	7.5
Ni	Tablet Level 1	9	9	8.63	7.3	1.8	(5.0, 10.8)	0.435	6.58	111.6
	Tablet Level 2	9	9	12.0	11	2	(8, 15)	0.641	10.55	106.2
	Tablet Level 3	9	9	15.3	18	1	(16, 20)	0.025	16.75	108.0
Pb	Tablet Level 1	9	9	2.53	2.3	1.2	(2.0, 2.6)	0.175	2.27	100.2
	Tablet Level 2	9	9	5.68	5.2	1.6	(3.9, 7.0)	0.598	6.67	78.4
	Tablet Level 3	9	9	14.8	15	1	(12, 19)	0.985	17.35	85.5
V	Tablet Level 1	9	9	22.6	17	2	(10, 29)	0.343	22.25	77.4
	Tablet Level 2	9	9	23.9	20	2	(12, 31)	0.426	22.7	86.4
	Tablet Level 3	9	9	1.31	1.9	2.3	(1.1, 3.3)	0.224	0.9	210.5

Table J1. Comparison of XRF values to Reference values

Analyte	Material	Total Measurements (n)	Measurements >LOQ (n)	Reference concentration (ug/g)	Mean concentration (ug/g)	Geometric standard dev (ug/g)	95% C	P value	Expected concentration (µg/g)	% of expected value
As	Tablet Level 1	9	9	6.05	5.6	1.0	(5.5, 5.7)	< 0.001	6.65	84.7
	Tablet Level 2	9	9	17.9	19	1	(18, 19)	0.078	19.8	93.8
	Tablet Level 3	9	9	43.6	48	1	(47, 50)	< 0.001	49.2	98.5
Cd	Tablet Level 1	9	9	1.97	2.5	1.2	(2.2, 2.9)	0.007	1.58	160.9
	Tablet Level 2	9	9	4.61	7.2	1.3	(6.1, 8.5)	< 0.001	5.26	136.1
	Tablet Level 3	9	9	11.5	18	1	(15, 22)	0.019	15.755	113.9
Co	Tablet Level 1	9	9	9.02	8.1	1.7	(5.8, 11.4)	0.568	8.68	93.7
	Tablet Level 2	9	9	20.3	22	1	(18, 27)	0.545	22.08	98.5
	Tablet Level 3	9	9	40.4	41	1	(38, 45)	0.534	50.12	82.7
Hg	Tablet Level 1	7	4	3.80	2.6	1.2	(2.2, 3.1)	0.026	6.48	40.0
	Tablet Level 2	7	4	14.2	3.4	1.2	(2.8, 4.2)	< 0.001	19.45	17.6
	Tablet Level 3	7	7	41.2	3.6	2.2	(2.1, 6.4)	< 0.001	48.609	7.5
Ni	Tablet Level 1	9	9	8.63	7.3	1.8	(5.0, 10.8)	0.435	6.58	111.6
	Tablet Level 2	9	9	12.0	11	2	(8, 15)	0.641	10.55	106.2
	Tablet Level 3	9	9	15.3	18	1	(16, 20)	0.025	16.75	108.0
Pb	Tablet Level 1	9	9	2.53	2.3	1.2	(2.0, 2.6)	0.175	2.27	100.2
	Tablet Level 2	9	9	5.68	5.2	1.6	(3.9, 7.0)	0.598	6.67	78.4
	Tablet Level 3	9	9	14.8	15	1	(12, 19)	0.985	17.35	85.5
V	Tablet Level 1	9	9	22.6	17	2	(10, 29)	0.343	22.25	77.4
	Tablet Level 2	9	9	23.9	20	2	(12, 31)	0.426	22.7	86.4
	Tablet Level 3	9	9	1.31	1.9	2.3	(1.1, 3.3)	0.224	0.9	210.5

One-sample t-test, mean XRF vs reference

More Information

Stephen W. Erickson, PhD
Senior Research Statistician
RTI International
serickson@rti.org