Appendix H

Positive Control Data

H1 Individual HET-CAM Egg Data for Dimethylformamide (provided by Drs. Vanparys and van Goethem) H-3

H2 Individual HET-CAM Egg Data for Imidazole (provided by Drs. Vanparys and van Goethem) H-7

H3 Individual HET-CAM Egg Data for Sodium Dodecyl Sulfate and Sodium Hydroxide (provided by Drs. Spielmann and Liebsch) H-11

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Appendix H1

Individual HET-CAM Egg Data for Dimethylformamide (provided by Drs. Vanparys and van Goethem)

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HET-CAM Test Scores for Dimethylformanide

Sequence Number	Hemorrhage Endpoint Score			Lysis Endpoint Score			Coagulation Endpoint Score			*In vitro* score		
	Egg 1	Egg 2	Egg 3	Egg 1	Egg 2	Egg 3	Egg 1	Egg 2	Egg 3	Egg 1	Egg 2	Egg 3
183	0.00	0.00	0.00	6.74	6.86	6.88	8.79	8.85	8.85	15.53	15.71	15.73
185	0.00	0.00	0.00	6.91	6.86	6.84	8.61	8.58	8.64	15.52	15.44	15.48
186	0.00	0.00	0.00	6.93	6.74	6.88	8.67	8.52	8.37	15.60	15.26	15.25
188	0.00	0.00	0.00	6.95	6.88	6.88	8.49	8.25	8.34	15.44	15.13	15.22
189	0.00	0.00	0.00	6.86	6.84	6.93	8.55	8.58	8.73	15.41	15.42	15.66
190	0.00	0.00	0.00	6.93	6.91	6.91	8.79	8.79	8.76	15.72	15.70	15.67
191	0.00	0.00	0.00	6.98	6.91	6.91	8.82	8.82	8.82	15.80	15.73	15.73
192	0.00	0.00	0.00	6.93	6.98	6.95	8.76	8.85	8.76	15.69	15.83	15.71
193	0.00	0.00	0.00	6.86	6.95	6.93	8.88	8.94	8.91	15.74	15.89	15.84
194	0.00	0.00	0.00	6.77	6.84	6.84	8.88	8.94	8.88	15.65	15.78	15.72
196	0.00	0.00	0.00	6.95	6.93	6.91	8.79	8.67	8.76	15.74	15.60	15.67
198	0.00	0.00	0.00	6.91	6.88	6.93	8.76	8.67	8.73	15.67	15.55	15.66
201	0.00	0.00	0.00	6.86	6.95	6.93	8.58	8.70	8.67	15.44	15.65	15.60
202	0.00	0.00	0.00	6.98	6.93	6.93	8.85	8.79	8.73	15.83	15.72	15.66
203	0.00	0.00	0.00	6.93	6.91	6.93	8.76	8.76	8.79	15.69	15.67	15.72
205	0.00	0.00	0.00	6.93	6.95	6.98	8.85	8.88	8.88	15.78	15.83	15.86
207	0.00	0.00	0.00	6.91	6.95	6.95	8.76	8.85	8.88	15.67	15.80	15.83
208	4.27	0.00	0.00	6.91	6.91	6.93	8.61	8.67	8.76	19.78	15.58	15.69
209	0.00	0.00	0.00	6.95	6.93	6.95	8.82	8.76	8.79	15.77	15.69	15.74
211	0.00	0.00	0.00	6.93	6.95	6.95	8.79	8.88	8.85	15.72	15.83	15.80
212	0.00	0.00	0.00	6.93	6.98	6.93	8.85	8.85	8.85	15.78	15.83	15.78
213	0.00	0.00	0.00	6.91	6.93	6.93	8.79	8.73	8.82	15.70	15.66	15.75
215	0.00	0.00	0.00	6.88	6.81	6.79	8.76	8.70	8.67	15.64	15.51	15.46
217	0.00	0.00	0.00	6.88	6.91	6.95	8.79	8.79	8.82	15.67	15.70	15.77
230	0.00	0.00	0.00	6.91	6.88	6.93	8.91	8.91	8.94	15.82	15.79	15.87
231	0.00	0.00	0.00	6.98	6.98	6.98	8.85	8.88	8.88	15.83	15.86	15.86
232	0.00	0.00	0.00	6.95	6.98	6.95	8.85	8.88	8.85	15.80	15.86	15.80
233	0.00	0.00	0.00	6.98	6.98	6.93	8.88	8.82	8.82	15.86	15.80	15.75
234	0.00	0.00	0.00	6.95	6.93	6.95	8.82	8.85	8.85	15.77	15.78	15.80
235	0.00	0.00	0.00	6.98	6.95	6.95	8.88	8.85	8.85	15.86	15.80	15.80
236	0.00	0.00	0.00	6.95	6.98	6.98	8.88	8.88	8.91	15.83	15.86	15.89
237	0.00	0.00	0.00	6.98	6.98	6.95	8.67	8.79	8.85	15.65	15.77	15.80
238	0.00	0.00	0.00	6.95	6.95	6.93	8.85	8.88	8.85	15.80	15.83	15.78
240	0.00	0.00	0.00	6.98	6.98	6.95	8.88	8.88	8.85	15.86	15.86	15.80
241	0.00	0.00	0.00	6.98	6.95	6.98	8.91	8.85	8.91	15.89	15.80	15.89
242	0.00	0.00	0.00	6.93	6.95	6.95	8.85	8.88	8.88	15.78	15.83	15.83
243	0.00	0.00	0.00	6.98	6.95	6.95	8.91	8.91	8.88	15.89	15.86	15.83
244	0.00	0.00	0.00	6.98	6.95	6.93	8.94	8.88	8.88	15.92	15.83	15.81
245	0.00	0.00	0.00	6.98	6.95	6.95	8.91	8.88	8.88	15.89	15.83	15.83
251	0.00	0.00	0.00	6.98	6.95	6.86	8.85	8.85	8.73	15.83	15.80	15.59
252	0.00	0.00	0.00	6.95	6.95	6.93	8.88	8.85	8.85	15.83	15.80	15.78
253	0.00	0.00	0.00	6.95	6.98	6.93	8.91	8.85	8.76	15.86	15.83	15.69

HET-CAM Test Scores for Dimethylformanide

Sequence Number	Hemorrhage Endpoint Score			Lysis Endpoint Score			Coagulation Endpoint Score			*In vitro* score		
	Egg 1	Egg 2	Egg 3	Egg 1	Egg 2	Egg 3	Egg 1	Egg 2	Egg 3	Egg 1	Egg 2	Egg 3
254	0.00	0.00	0.00	6.95	6.88	6.91	8.88	8.73	8.82	15.83	15.61	15.73
255	0.00	0.00	0.00	6.93	6.93	6.93	8.82	8.76	8.85	15.75	15.69	15.78
256	0.00	0.00	0.00	6.95	6.95	6.93	8.88	8.85	8.85	15.83	15.80	15.78
257	0.00	0.00	0.00	6.91	6.93	6.95	8.82	8.85	8.85	15.73	15.78	15.80
258	0.00	0.00	0.00	6.98	6.95	6.95	8.88	8.82	8.85	15.86	15.77	15.80
259	0.00	0.00	0.00	6.95	6.88	6.95	8.88	8.76	8.91	15.83	15.64	15.86
260	0.00	0.00	0.00	6.95	6.95	6.93	8.88	8.85	8.82	15.83	15.80	15.75
261	0.00	0.00	0.00	6.98	6.95	6.93	8.91	8.85	8.82	15.89	15.80	15.75
262	0.00	0.00	0.00	6.95	6.95	6.93	8.88	8.85	8.88	15.83	15.80	15.81
263	0.00	0.00	0.00	6.95	6.91	6.95	8.88	8.85	8.85	15.83	15.76	15.80
264	0.00	0.00	0.00	6.95	6.98	6.98	8.88	8.85	8.88	15.83	15.83	15.86
265	0.00	0.00	0.00	6.98	6.95	6.95	8.91	8.85	8.88	15.89	15.80	15.83
266	0.00	0.00	0.00	6.95	6.93	6.79	8.85	8.82	8.61	15.80	15.75	15.40
267	0.00	0.00	0.00	6.95	6.95	6.93	8.82	8.85	8.85	15.77	15.80	15.78
268	0.00	0.00	0.00	6.95	6.95	6.95	8.88	8.91	8.88	15.83	15.86	15.83
269	0.00	0.00	0.00	6.95	6.95	6.95	8.91	8.88	8.88	15.86	15.83	15.83
270	0.00	0.00	0.00	6.93	6.95	6.95	8.85	8.88	8.91	15.78	15.83	15.86
271	0.00	0.00	0.00	6.95	6.93	6.93	8.82	8.85	8.85	15.77	15.78	15.78
272	0.00	0.00	0.00	6.91	6.98	6.95	8.73	8.85	8.85	15.64	15.83	15.80
273	0.00	0.00	0.00	6.93	6.98	6.93	8.82	8.88	8.85	15.75	15.86	15.78
274	0.00	0.00	0.00	6.95	6.91	6.95	8.88	8.79	8.91	15.83	15.70	15.86
275	0.00	0.00	0.00	6.95	6.98	6.95	8.91	8.88	8.88	15.86	15.86	15.83
277	0.00	0.00	0.00	6.86	6.91	6.93	8.73	8.82	8.85	15.59	15.73	15.78
278	0.00	0.00	0.00	6.95	6.91	6.95	8.82	8.79	8.85	15.77	15.70	15.80
279	0.00	0.00	0.00	6.93	6.93	6.93	8.85	8.79	8.85	15.78	15.72	15.78
280	0.00	0.00	0.00	6.93	6.95	6.81	8.85	8.88	8.70	15.78	15.83	15.51
282	0.00	0.00	0.00	6.95	6.91	6.91	8.88	8.82	8.85	15.83	15.73	15.76
1A[1]	3.48	3.63	3.38	6.81	6.74	6.79	8.82	8.82	8.85	19.11	19.19	19.02
1B	3.35	3.15	4.02	6.65	6.74	6.67	8.88	8.91	8.85	18.88	18.80	19.54
2A	2.98	2.72	3.18	5.72	6.23	6.39	8.67	8.70	8.70	17.37	17.65	18.27
2B	3.77	3.98	3.98	6.56	6.58	6.72	8.79	8.82	8.88	19.12	19.38	19.58
3A	2.93	3.18	3.18	6.42	6.51	6.60	8.88	8.79	8.76	18.23	18.48	18.54
4A	3.20	3.33	3.38	6.46	6.49	6.63	8.76	8.82	8.82	18.42	18.64	18.83
4B	3.62	3.47	3.58	6.56	6.70	6.67	8.73	8.79	8.82	18.91	18.96	19.07
6A	2.02	2.58	3.97	6.70	4.90	5.86	8.76	8.82	8.88	17.48	16.30	18.71
8A-10A	3.97	2.60	3.02	6.65	6.88	6.91	8.76	8.82	8.88	19.38	18.30	18.81
11A	3.38	3.92	3.82	6.84	6.93	6.91	8.73	8.85	8.82	18.95	19.70	19.55
133	4.20	3.97	4.00	6.79	6.86	6.88	8.70	8.79	8.88	19.69	19.62	19.76
16-17-18	4.07	3.95	3.80	6.84	6.88	6.77	8.73	8.79	8.67	19.64	19.62	19.24

[1] Test Method Data 183 to 282 represent studies where a Test Substance Applicator was used and the hemorrhage endpoint was evaluated inside of the Test Substance Applicator.

[2] Test Method Data 1A to 11A represent studies where a Test Substance Applicator was used and the hemorrhage endpoint was evaluated outside of the Test Substance Applicator.

[3] Test Method Data 133 to 16-17-18 represent studies where a Test Substance Applicator was not used.

Appendix H2

Individual HET-CAM Egg Data for Imidazole (provided by Drs. Vanparys and van Goethem)

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HET-CAM Test Scores for Imidazole

Sequence Number	Hemorrhage Endpoint Score			Lysis Endpoint Score			Coagulation Endpoint Score			*In vitro* score		
	Egg 1	Egg 2	Egg 3	Egg 1	Egg 2	Egg 3	Egg 1	Egg 2	Egg 3	Egg 1	Egg 2	Egg 3
186	3.40	4.83	4.83	6.84	6.84	6.79	8.31	8.43	8.46	18.55	20.10	20.08
190	4.92	4.92	4.88	6.93	6.93	6.88	8.73	8.79	8.70	20.58	20.64	20.46
194	4.03	4.45	4.32	6.70	6.81	6.84	8.85	8.85	8.88	19.58	20.11	20.04
214	4.03	3.88	3.95	6.88	6.88	6.91	8.76	8.73	8.79	19.67	19.49	19.65
220	4.30	4.48	4.25	6.95	6.79	6.88	8.79	8.58	8.76	20.04	19.85	19.89
269	4.03	4.02	3.47	6.95	6.91	6.91	8.73	8.70	8.76	19.71	19.63	19.14
270	4.13	3.88	4.00	6.67	6.72	6.81	8.25	8.22	8.46	19.05	18.82	19.27
274	4.18	4.20	4.37	6.77	6.86	6.86	8.52	8.52	8.58	19.47	19.58	19.81
278	4.67	4.68	4.45	6.88	6.93	6.93	8.76	8.79	8.82	20.31	20.40	20.20
281	4.57	4.57	4.55	6.93	6.91	6.93	8.76	8.73	8.76	20.26	20.21	20.24
5A	4.85	4.88	4.90	6.58	6.65	6.74	8.85	8.88	8.91	20.28	20.41	20.55
7A-9A	4.93	4.95	4.95	6.84	6.88	6.88	8.55	8.43	8.49	20.32	20.26	20.32
12A	4.92	4.93	4.93	6.81	6.84	6.79	8.61	8.55	8.46	20.34	20.32	20.18
13	4.92	4.95	4.92	6.84	6.91	6.81	8.40	8.76	8.55	20.16	20.62	20.28
14	4.78	4.77	4.73	6.88	6.84	6.88	8.85	8.73	8.85	20.51	20.34	20.46

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Appendix H3

Individual HET-CAM Egg Data for Sodium Dodecyl Sulfate and Sodium Hydroxide (provided by Drs. Spielmann and Liebsch)

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German HET-CAM Validation Study: Retrospective Analysis of Positive Controls (1% SLS and 0.1n NaOH), concurrently tested with coded test chemicals

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DATA SET USED FOR ANLAYSIS

In the German Validation Study, 1% SLS and 0.1 NaOH served as Positive Controls (PC). They were concurrently tested with the test chemicals and used as acceptance criteria for the results. For the purpose of the present assessment of intra- and interlaboratory variability of the HET-CAM, PC data of 105 coded test chemicals were analysed. This amounts to about 2/3 of the total of 150 chemicals that were tested in phase II (data base development) of the German validation study.

Since each test chemical was tested on two independent runs (run 1 and run 2) and in two different laboratories (lab 1 and lab 2), in theory, four sets of SLS data and four sets of NaOH data were generated together with each coded test chemical. In practice, however, one PC sometimes served for more then one test chemical, and is therefore only listed in the files of one of the coded chemicals.

Since each coded test chemical was randomly assigned (by a computer) to be tested in two of the 12 participating laboratories, in the present analysis, "lab1" is representing the total of all 12 participating labs, and "lab2" as well. Using these randomly generated "virtual laboratories 1 and 2" for the interlaboratory analysis, is a compromise, due to the fact that data had to be extracted from coded test chemical files in our archieves from paper hardcopies. Decoding all info and assigning the data to the 12 individual laboratories would have been too much work. However, from a biostatistical standpoint, the random generation of assignments of the 12 laboratories allows application of the procedures described below.

BIOSTATISTICAL PROCEDURES

The GLM (General Linear Model) Multivariate procedure was used for analysis of inter- and intra- laboratory variances. The advantage of this procedure is, that it provides the analysis of variance for multiple dependent variables by one or more factors.

Each level of a factor can have a different linear effect on the value of the dependent variables. The GLM Multivariate procedure assumes that all the model factors are fixed; that is, they are generally thought of as variables whose values of interest are all represented in the data file, usually by design.

In the HET-CAM the dependent variables are *haemorrhage*, *coagulation*, *vessel lysis* and the factors are "*laboratories*" (interlaboratory reproducibility) and "*runs*" (intralaboratory repeatability over time). Per each of the two positive control chemicals SLS and NaOH, values obtained for *haemorrhage*, *coagulation*, and *vessel lysis* were used for determination of the

statistical variability between "laboratories" and “runs”. Intralaboratory and interlaboratory differences are regarded significant if the error probability values $p < 0.05$.

RESULTS

Table 1 shows the means ± standard deviation for the parameters *haemorrhage*, *coagulation*, and *vessel lysis* as observed for the two PC's, 1% SLS and 0.1n NaOH. From these data it is already obvious that differences between labs are not likely. *Note*: Coagulation does not occur upon exposure with 0.1% SLS. It was, however, in one single case, observed. Since non existing values were calculated with the arbitrary value "0", the mean ± SD marked yellow are meaningless.

Table 2 shows, for each of the three parameters *haemorrhage*, *coagulation*, and *vessel lysis* the means and lower / upper boundaries of the 95% confidence intervals. Confidence intervals are sufficiently narrow, and do not show obvious differences between the laboratories 1 and 2.

Figure 1 and **Figure 2** are visualisations of the content of **Table 1** showing, separately for the two PC's 0.1n NaOH and 1% SLS the variability measures (SD) obtained in lab 1 and lab 2 for the three parameters *haemorrhage*, *coagulation*, and *vessel lysis.*

The results of the GLM Multivariate procedure is given in **Table 3 and 4**. Each multivariate statistic is transformed into a test statistic with an approximate or exact F distribution, given as F. The variances can be divided up and can be computed as the sum of squared deviations (Sums of squares) from the overall mean. Although there are n levels of each factor, one degree of freedom is lost because of the deviations are subject to one constraint. Therefore, the degrees of freedom are n-1.

In summary, no significant differences between runs in the two laboratories were determined indicating a very good intra-laboratory performance of the assay. The differences between laboratories were very low and not significant for the three endpoint values haemorrage and coagulation and vessel lysis. Therefore we conclude that the assay proved sufficient reliability.

Table 1: **Mean and standard deviation (SD) for the endpoint values haemorrage, coagulation and vessel lysis (detection time in [sec])**

Endpoint	CHEMICAL	LAB	Mean	Std. Deviation	n
haemorrage	0.1n NaOH	1	9.16	6.491	176
		2	8.74	2.294	160
		Total	8.96	4.955	336
	1% SLS	1	15.16	5.812	206
		2	14.12	4.711	171
		Total	14.69	5.359	377
coagulation	0.1n NaOH	1	51.02	35.907	176
		2	44.76	32.816	160
		Total	48.04	34.561	336
	1% SLS	1	.00	.000	206
		2	.35	4.588	171
		Total	.16	3.090	377
vessel lysis	0.1n NaOH	1	37.99	24.433	176
		2	32.98	24.816	160
		Total	35.60	24.707	336
	1% SLS	1	36.50	17.060	206
		2	33.60	17.179	171
		Total	35.18	17.152	377

Table 2: **Mean, standard error and 95% Confidence Interval for the endpoint values *haemorrhage*, *coagulation* and *vessel lysis* (detection time in [sec])**

Endpoint	CHEMICAL				95% Confidence Interval	
		LAB	Mean	std. error	Lower Bound	Upper Bound
haemorrage	0.1n NaOH	1	**9.165**	.389	**8.401**	**9.929**
		2	**8.738**	.408	**7.936**	**9.539**
	1% SLS	1	**15.155**	.360	**14.449**	**15.862**
		2	**14.123**	.395	**13.347**	**14.898**
coagulation	0.1n NaOH	1	**51.023**	1.791	**47.506**	**54.540**
		2	**44.763**	1.879	**41.074**	**48.451**
	1% SLS	1	**.000**	1.656	**-3.251**	**3.251**
		2	**.351**	1.817	**-3.217**	**3.919**
vessel lysis	0.1n NaOH	1	**37.994**	1.582	**34.889**	**41.100**
		2	**32.975**	1.659	**29.718**	**36.232**
	1% SLS	1	**36.495**	1.462	**33.625**	**39.366**
		2	**33.602**	1.605	**30.452**	**36.753**

Figure 1: **Error bars of the endpoint values haemorrage, coagulation and vessel lysis (detection time in [sec]) ± standard deviation for 0.1n NaOH**

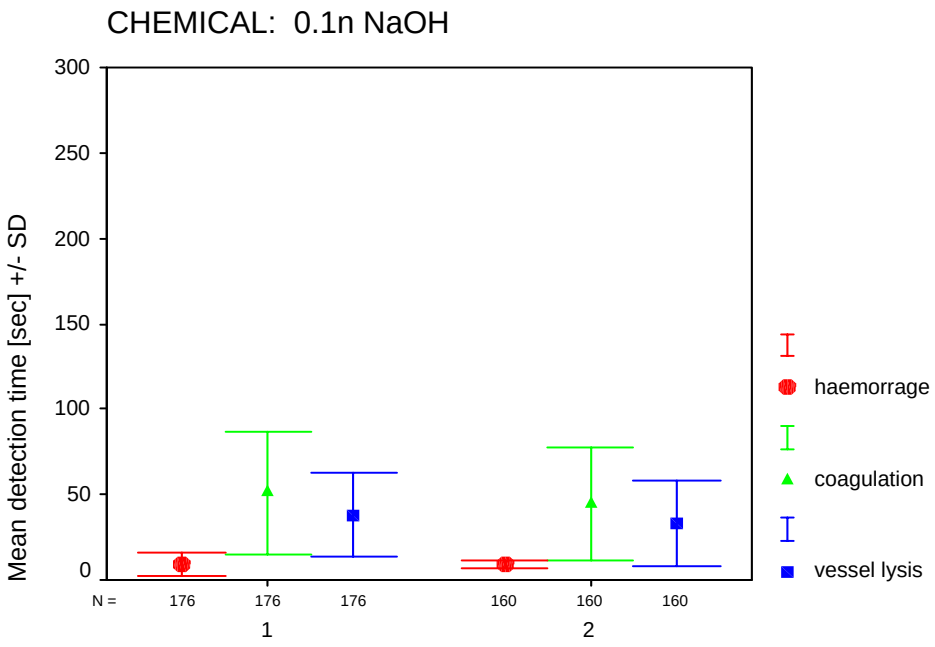

Figure 2: **Error bars of the endpoint values haemorrage, coagulation and vessel lysis (detection time in [sec] +/- Standard deviation (SD) for 1% SLS**

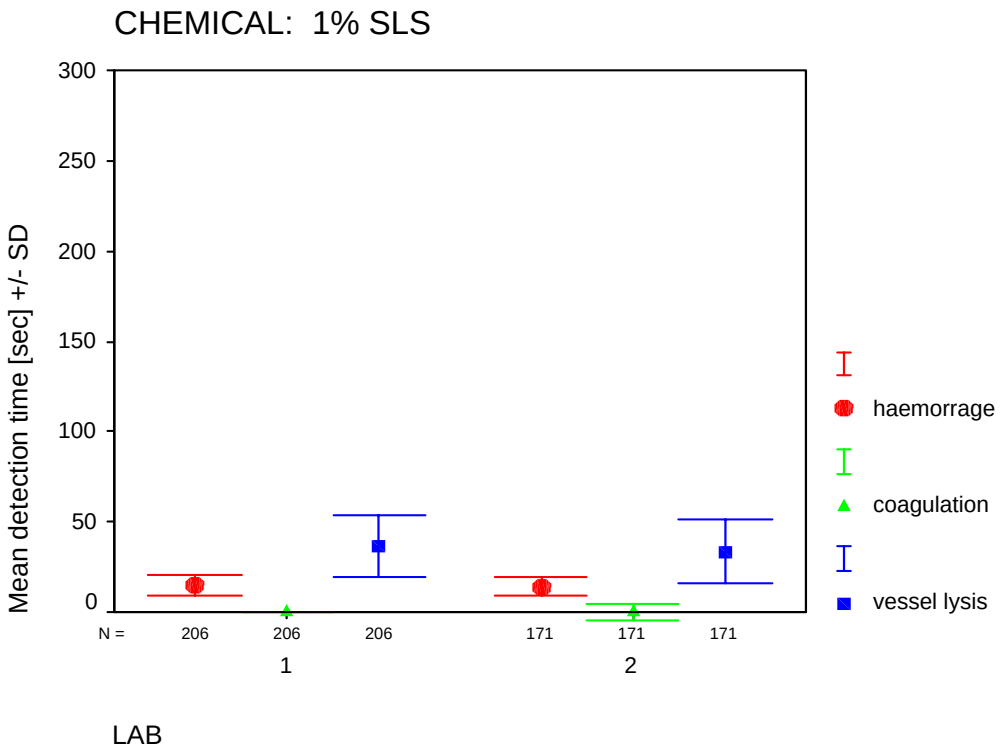

Table 3: **Results of the GLM (General Linear Model) Multivariate procedure for analysis of inter- and intra- laboratory variances for <u>Positive Control 0.1n NaOH</u>**
Sig. = significance = p value

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.
LAB	haemorrage	15,326	1	15,326	,622	,431
	coagulation	3284,037	1	3284,037	2,756	,098
	vessel lysis	2113,058	1	2113,058	3,481	,063
RUN	haemorrage	8,489	1	8,489	,345	,558
	coagulation	14,236	1	14,236	,012	,913
	vessel lysis	235,342	1	235,342	,388	,534
Error	haemorrage	8200,708	333	24,627		
	coagulation	396836,648	333	1191,702		
	vessel lysis	202147,552	333	607,050		
Total	haemorrage	35207,000	336			
	coagulation	1175624,00	336			
	vessel lysis	630427,000	336			

No significant differences between laboratories (Interlaboratory) and independent runs (intralaboratory) within a laboratory

Table 4: **Results of the GLM (General Linear Model) Multivariate procedure for analysis of inter- and intra- laboratory variances for <u>Positive Control 1% SDS</u>**

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.
LAB	haemorrage	99,599	1	99,599	3,482	,063
	coagulation	11,484	1	11,484	1,203	,273
	vessel lysis	781,086	1	781,086	2,666	,103
RUN	haemorrage	,861	1	,861	,030	,862
	coagulation	9,890	1	9,890	1,036	,309
	vessel lysis	253,701	1	253,701	,866	,353
Error	haemorrage	10696,589	374	28,601		
	coagulation	3569,057	374	9,543		
	vessel lysis	109576,753	374	292,986		
Total	haemorrage	92119,000	377			
	coagulation	3600,000	377			
	vessel lysis	577280,000	377			

Sig. = significance = p value
No significant differences between laboratories (Interlaboratory) and independent runs (intralaboratory) within a laboratory

Test	1% SLS												0.1n NaOH											
Chem	Laboratory 1						Laboratory 2						Laboratory 1						Laboratory 2					
Code	run1			run2			run1			run2			run1			run2			run1			run2		
	H	C	L	H	C	L	H	C	L	H	C	L	H	C	L	H	C	L	H	C	L	H	C	L
51	9	-	14	14	-	21	18	-	55	16	-	34	8	42	10	11	44	13	14	24	36	10	15	27
53	22	-	47	13	-	24	15	-	22	14	-	22	6	38	-	9	25	-	8	21	14	8	22	13
54	18	-	55	16	-	34	13	-	22	15	-	24	14	24	36	10	15	27	9	23	13	9	19	13
59	17	-	28	18	-	33	13	-	18	10	-	17	11	17	28	12	16	30	8	47	12	7	34	13
60	15	-	22	14	-	22	19	-	78	9	-	65	8	21	14	8	22	13	9	44	61	8	14	88
64	13	-	56	11	-	34	11	-	17	9	-	14	9	38	53	7	53	54	7	41	14	7	46	14
65	10	-	81	9	-	65	10	-	17	13	-	19	5	49	72	8	14	88	9	52	17	6	42	9
66	13	-	35	13	-	22	9	-	65	10	-	76	11	110	20	8	118	41	4	39	74	8	20	87
67	19	-	28	13	-	30	10	-	76	12	-	70	9	82	20	9	92	18	8	20	87	7	15	93
68	25	-	34	13	-	24	21	-	45	15	-	34	11	44	-	9	25	-	12	19	44	12	19	31
72	11	-	86	10	-	76	10	-	15	9	-	14	5	37	104	8	20	87	8	48	12	7	36	13
73	16	-	37	15	-	36	15	-	22	14	-	22	16	24	44	9	15	30	8	21	14	8	22	13
74	26	-	46	21	-	25	12	-	23	17	-	25	10	31	-	10	29	-	8	161	19	7	168	22
75	13	-	58	11	-	34	26	-	46	16	-	34	9	49	66	7	53	54	10	31	-	9	41	-
76	21	-	39	19	-	29	13	-	18	14	-	21	9	33	-	9	45	-	7	28	11	7	31	13
79	15	-	51	18	-	38	17	-	28	18	-	33	10	58	65	10	44	73	11	17	28	12	16	30
80	10	-	76	12	-	70	13	-	18	14	-	21	8	20	87	7	15	93	7	28	11	7	31	13
81	13	-	18	14	-	21				15	-	28	7	28	11	7	31	13				11	76	25
83	16	-	34	17	-	34	14	-	24	17	-	56	12	18	29	10	17	31	7	131	20	10	99	25
84	21	-	39	21	-	25	13	-	18	14	-	21	9	33	-	10	29	-	7	28	11	7	31	13
85	9	-	55	12	-	71							5	17	73	5	21	78						
89	15	-	21	13	-	17	12	-	25	13	-	26	9	39	13	11	52	13	10	163	34	11	104	24
90	12	-	25	12	-	22	14	-	49	11	-	64	9	109	31	10	162	40	10	75	48	8	61	70
91	18	-	34	21	-	31							10	17	33	13	18	30						

96	9	-	36	10	-	25	18	-	36	19	-	36	10	97	25	6	131	18	7	19	29	13	23	34
98	16	-	33	18	-	30	16	-	23	13	-	22	9	13	27	13	18	34	8	15	11	9	21	15
101	16	-	23	13	-	22	17	-	20	13	-	17	8	15	11	9	2	15	8	56	17	10	49	12
102	9	-	55	13	-	54	18	-	34	19	-	36	5	17	73	5	21	64	10	17	33	13	23	34
105	13	-	51	11	-	49	16	-	23	13	-	22	9	48	68	7	54	70	8	15	11	9	21	15
105	11	-	29	13	-	26	16	-	21	14	-	19	9	79	25	7	91	38	12	74	15	10	68	14
107	20	-	41	20	-	39							10	20	33	16	20	39						
108	17	-	44	7	-	41	13	-	19	14	-	18	11	49	56	7	51	58	12	41	15	11	50	16
109	9	-	55	13	-	54	16	-	23	13	-	22	5	17	73	5	21	64	8	15	11	9	21	15
110	20	-	59	14	-	51	11	-	24	13	-	60	7	27	77	5	80	82	7	40	51	7	45	61
111	12	-	31	13	-	27	13	-	35				11	104	24	9	181	22	9	110	23			
113	10	-	25	13	-	29	17	-	41	20	-	37	6	150	18	7	95	48	15	27	47	10	10	31
114	23	-	38	20	-	37							9	18	30	10	20	31						
116	13	-	76	17	-	69							8	23	104	4	17	75						
117	20	-	59	9	-	55	13	-	74	11	-	49	7	27	77	5	17	73	8	57	47	7	54	70
118	10	-	36	22	-	41	14	-	68	12	-	54	16	24	33	15	21	36	8	39	81	5	21	64
119	12	-	52	10	-	55	13	-	35	9	-	36	7	45	75	7	51	61	9	107	23	10	97	25
122	16	-	32	13	-	22							8	15	11	9	21	15						
123	14	-	25	16	-	30							10	120	128	10	104	30						
125	11	-	32	11	-	52	18	-	66	14	-	34	7	41	53	7	57	72	11	17	42	9	21	36
126	22	-	27	12	-	24	19	-	44	30	60	90	7	71	17	10	85	12	9	18	-	8	48	-
127	19	-	44	16	-	30							9	18	-	10	31	-						
128	13	-	59				16	-	18	15	-	21	5	35	73				12	57	16	10	35	16
130	7	-	16	11	-	25	10	-	17	14	-	17	8	107	16	9	76	19	8	23	12	10	29	17
131	19	-	44	16	-	30	16	-	32	16	-	37	9	18	-	10	31	-	9	19	33	10	22	31
132	19	-	44	30	-	75	16	-	18	15	-	21	9	18	-	8	48	-	12	57	16	10	35	16
133	19	-	44	30	-	75	10	-	78	11	-	68	9	18	-	8	48	-	4	21	91	8	38	77
135	16	-	18	15	-	21	11	-	17	9	-	17	12	57	16	10	35	16	11	47	14	7	50	10

136	18	-	66	18	-	38	10	-	21	10	-	45	11	17	42	10	17	36	9	72	19	8	95	20
140	12	-	18	11	-	17							9	44	13	8	27	13						
143	9	-	21	11	-	23	7	-	21	11	-	31	7	104	15	8	103	33	6	52	53	9	41	70
145	10	-	21	13	-	28	9	-	17	14	-	20	9	72	19	8	99	24	7	50	10	9	47	14
146	18	-	38	13	-	36							10	17	36	13	22	38						
147	12	-	25	9	-	26	12	-	72				7	43	53	5	40	55	8	37	88			
148	14	-	57	12	-	46	19	-	44	28	-	54	7	57	68	8	31	58	9	18	-	9	47	-
149	11	-	20	13	-	23	12	-	30	16	-	39	11	48	17	11	48	18	12	22	35	16	22	36
150	14	-	73				19	-	51	14	-	60	5	24	73				7	56	47	11	53	59
151	18	-	65	6	-	27	15	-	22	12	-	19	7	54	54	8	54	62	10	43	18	11	44	15
154	11	-	23	7	-	19	14	-	37	16	-	36	8	103	33	7	117	19	8	15	29	10	19	23
156	11	-	43	13	-	39	12	-	31	14	-	32	9	42	62	7	44	67	7	14	27	10	17	33
159	16	-	23	9	-	21							8	88	20	9	121	35						
160	10	-	32	9	-	26	14	-	19	17	-	20	9	43	54	7	44	61	10	60	13	10	58	12
161	18	-	22	15	-	23							7	22	12	7	21	22						
163	14	-	31	14	-	30	18	-	22	15	-	23	9	13	29	9	15	33	7	22	12	7	21	12
164	23	-	36	22	-	40	9	-	37	9	-	26	15	37	-	13	36	-	10	43	64	7	44	61
165	9	-	52				13	-	18	13	-	18	4	17	84				10	59	14	10	57	13
168	10	-	31	15	-	15	15	-	20	13	-	19	6	67	20	9	141	24	12	62	15	10	57	12
171	10	-	31	15	-	25	18	-	22	15	-	23	6	67	20	9	143	24	7	22	12	7	21	12
172	12	-	30	12	-	64	11	-	22	10	-	24	6	58	55	7	59	69	8	90	26	8	114	26
173	30	-	50	41	-	71	10	-	51				9	34	-	25	49	-	4	22	89			
174	9	-	27	13	-	48	8	-	52	9	-	71	7	43	50	6	35	47	4	18	76	4	21	77
175	10	-	15	13	-	23	6	-	53				7	42	10	7	47	12	4	26	94			
177	30	-	50	41	-	71	14	-	34	15	-	30	9	34	-	25	49	-	13	20	32	8	15	30
178	15	-	34	15	-	39	7	-	33	9	-	23	13	20	32	9	17	31	6	27	49	6	29	43
180	12	-	16	12	-	16	15	-	21	14	-	18	8	31	11	8	21	11	9	54	13	11	52	15
182	30	-	50	41	-	71	12	-	30	13	-	3	9	34	-	25	49	-	10	21	34	10	17	29

184	19	-	53	22	-	61	12	-	62	13	-	48	9	98	29	10	85	35	7	48	46	6	35	47
187	18	-	100	18	-	79	12	-	16	12	-	16	10	143	94	10	16	52	8	31	11	8	21	11
188	15	-	21	15	-	19	33	-	48	33	-	48	12	43	15	8	31	11	11	32	-	11	32	-
189	10	-	37	10	-	42	29	-	51	29	-	51	4	32	49	6	29	46	11	26	-	11	26	-
190	15	-	19	16	-	21	10	-	56	12	-	53	89	31	11	8	37	10	5	29	98	4	23	85
192	11	-	21	12	-	20	15	-	19	14	-	20	14	117	24	12	90	28	8	31	11	9	35	11
193	33	-	48	33	-	52	12	-	33	8	-	22	11	32	-	9	28	-	6	43	54	7	45	61
195	15	-	21	14	-	20	10	-	51				12	43	15	9	35	11	6	21	75			
196	13	-	30	14	-	38							10	19	32	11	18	31						
198	11	-	28	11	-	33	17	-	31	15	-	22	6	35	44	9	35	52	13	74	16	9	58	16
199	15	-	21	14	-	20							12	43	15	9	35	11						
201	12	-	25	13	-	24	29	-	51	29	-	51	7	79	19	9	121	32	11	26	-	11	26	-
202	17	-	50				17	-	21	15	-	22	11	22	58				13	74	16	9	58	16
203	16	-	21	14	-	19	12	-	25	15	-	27	12	74	15	10	68	14	7	79	19	15	88	44
204	9	-	28	13	-	47	13	-	30	10	-	29	6	31	43	8	34	50	10	19	32	9	17	30
206	13	-	24	11	-	27	7	-	54	5	-	68	9	101	32	10	94	24	6	21	109	5	21	117
207	15	-	19	14	-	20	11	-	32	11	-	23	8	31	11	9	32	11	9	79	23	10	97	20
210	13	-	47	8	-	22	14	-	36	16	-	38	8	34	50	8	28	38	8	16	30	8	17	33
211	14	-	36	16	-	38							8	16	30	8	17	33						
212	18	-	40	18	-	40	14	-	38	13	-	28	8	18	-	8	18	-	11	18	31	12	22	36
214	17	-	22	15	-	19	9		27	12	-	25	12	68	16	11	73	14	6	111	35	10	151	26
215	29	-	14	14	-	19	13	-	24	10	-	27	9	70	15	10	63	13	9	118	29	10	117	35
216	14	-	21	13	-	21							10	65	17	10	66	17						
219	17	-	28	11	-	30	13	-	22	13	-	21	7	85	21	12	83	29	9	21	15	6	17	11
223	14	-	18	13	-	17	11	-	24	13	-	29	10	50	14	10	49	12	8	101	24	11	98	46

H = haemorrage; C = coagulation; L = vessel lysis;
detection time of endpoints [sec];
Positive Controls for 105 of 150 coded phase II chemicals were randomly extracted