**Supplemental Tables**

**Supplemental Table 1.** Total analytical CV (include both within- and between-run variation)

based upon analyses of internal controls.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Pathological control** | | **Normal control** | |
| **Parameter** | **Mean value** | **Total analytical**  **CV (%)** | **Mean value** | **Total analytical CV (%)** |
| **APTT1** | 46.7 seconds | 4.7 | 39.7 seconds | 3.1 |
| **APTT2** | 42.9 seconds | 3.3 | 36.0 seconds | 2.6 |
| **INR1** | 3.26 ratio | 3.5 | 1.01 ratio | 2.6 |
| **INR2** | ratio | 3.3 | 1.12 ratio | 2.0 |
| **Fibrinogen** | 1.16 g/L | 4.1 | 3.04 g/L | 3.3 |
| **FVIII:C** | 45% | 10.9 | 96% | 12.4 |
| **vWF:Ag** | 34% | 6.4 | 85% | 4.0 |

CV, coefficient of variation, APTT, Activated Partial Thromboplastin Time, PT, Prothrombin Time,

INR, International Normalized Ratio, FVIII:C, Factor VIII clot, vWF:Ag, von Willebrand factor antigen.

**Supplemental Table 2.** Within-run analytical variation (CVA) for the original results of

duplicate participants’ samples (all duplicate results included).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Pregnant** | | **Non-pregnant** | |
| **Parameter** | **Mean value** | **Within-run CV (%) (CVA)** | **Mean value** | **Within-run CV (%) (CVA)** |
| **APTT1** | 32.6 seconds | 0.7 | 34.7 seconds | 0.8 |
| **APTT2** | 29.5 seconds | 0.8 | 28.6 seconds | 0.9 |
| **PT1** | 25.3 seconds | 1.0 | 28.6 seconds | 0.9 |
| **PT2** | 13.6 seconds | 0.7 | 13.6 seconds | 0.7 |
| **INR1** | 0.97 (ratio) | 1.0 | 1.06 (ratio) | 0.9 |
| **INR2** | 1.06 (ratio) | 0.8 | 1.06 (ratio) | 0.7 |
| **Fibrinogen** | 3.8 g/L | 2.6 | 2.9 g/L | 2.2 |
| **FVIII:C** | 208% | 4.2 | 118% | 2.9 |
| **vWF:Ag** | 158% | 2.5 | 87% | 3.0 |

CV, coefficient of variation, APTT, Activated Partial Thromboplastin Time, PT, Prothrombin Time,

INR, International Normalized Ratio, FVIII:C, Factor VIII clot, vWF:Ag, von Willebrand factor antigen.

**Supplemental Table 3.** P-values aftertesting ofGaussian distribution and variance homogeneity for five different coagulation parameters in pregnancy (9 samples), for MoM, lnMoM and lnMoM after exclusion of outliers.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **MoM** | | | | | | | | |
| MoM | **APTT1** | **APTT2** | **PT1** | **PT2** | **INR1** | **INR2** | **Fibrinogen** | **FVIII:C** | **vWF:Ag** |
| **Variance homogeneity** | 0.02 | 0.78 | 0.34 | 0.13 | 0.04 | 0.14 | <0.001 | <0.001 | <0.001 |
| **Gaussian distribution** | 0.27 | 0.41 | 0.01 | <0.001 | 0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| lnMoM | **lnMoM** | | | | | | | | |
| **Variance homogeneity** | 0.02 | 0.80 | 0.35 | 0.19 | 0.05 | 0.20 | <0.001 | <0.001 | <0.001 |
| **Gaussian distribution** | 0.32 | 0.53 | 0.05 | <0.001 | 0.02 | <0.001 | <0.001 | <0.001 | 0.001 |
| lnMoM without outliers | **lnMoM excluding outliersa** | | | | | | | | |
| **Variance homogeneity** | 0.02 | 0.80 | 0.15 | 0.44 | 0.33 | 0.59 | 0.01 | <0.001 | 0.02 |
| **Gaussian distribution** | 0.32 | 0.53 | 0.05 | 0.17 | 0.41 | 0.13 | 0.29 | 0.03 | 0.22 |

aSee materials and methods for outliers.

Significance level p≥0.01 (green) and p <0.01 (red), Bartlett’s test (variance homogeneity) and Shapiro-Wilk test (Gaussian distribution).

APTT, Activated Partial Thromboplastin Time, PT, Prothrombin Time, INR, International Normalized Ratio, FVIII:C, Factor VIII clot, vWF:Ag, von Willebrand factor antigen.

**Supplemental Table 4.** P-values aftertesting ofGaussian distribution and variance homogeneity for different coagulation parameters in nonpregnant (10 samples), for MoM, lnMoM and lnMoM after exclusion of outliers.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **MoM** | | | | | | | | |
| MoM | **APTT1** | **APTT2** | **PT1** | **PT2** | **INR1** | **INR2** | **Fibrinogen** | **FVIII:C** | **vWF:Ag** |
| **Variance homogeneity** | 0.16 | 0.16 | 0.35 | 0.06 | 0.42 | 0.03 | 0.02 | 0.05 | 0.003 |
| **Gaussian distribution** | 0.33 | 0.42 | 0.07 | 0.51 | 0.40 | 0.08 | <0.001 | <0.001 | <0.001 |
| lnMoM | **lnMoM** | | | | | | | | |
| **Variance homogeneity** | 0.17 | 0.17 | 0.39 | 0.06 | 0.44 | 0.03 | 0.04 | 0.16 | 0.006 |
| **Gaussian distribution** | 0.25 | 0.37 | 0.07 | 0.69 | 0.36 | 0.72 | 0.001 | 0.002 | 0.13 |
| lnMoM without outliers | **lnMoM excluding outliers** a | | | | | | | | |
| **Variance homogeneity** | NA | NA | NA | NA | NA | NA | 0.06 | 0.54 | 0.10 |
| **Gaussian distribution** | NA | NA | NA | NA | NA | NA | 0.02 | 0.19 | 0.33 |

aSee materials and methods for outliers.

Significance level p≥0.01 (green) and p <0.01 (red), Bartlett’s test (variance homogeneity) and Shapiro-Wilk test (Gaussian distribution).

APTT, Activated Partial Thromboplastin Time, PT, Prothrombin Time, INR, International Normalized Ratio, FVIII:C, Factor VIII clot, vWF:Ag, von Willebrand factor antigen. NA, not applicable (no outliers were excluded).

**Supplemental Table 5.** Within- (CVI) and between- (CVG) subject biological variation based upon both original results of coagulation tests and upon lnMoM results for pregnant (9 samples), pregnant and postpartum (12 samples) and non-pregnant women.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Parameter** | **Number of samples** | **Based on original results** | **Based on lnMoM** | **Based on original results** | **Based on the lnMoM** |
| **Pregnant** | **CVI % (95%CI)** | **CVI % (95%CI)** | **CVG %(95%CI)** | **CVG % (95%CI)** |
| **APTT1** | 9 samples | 4.2 (3.8-4.8) | 3.0 (2.7-3.4) | 5.3 (3.9-7.9) | 5.3 (4.0-7.9) |
| 12 samples | 5.0 (4.5-5.5) | 3.8 (3.5-4.2) | 4.7 (3.5-7.1) | 4.9 (3.7-7.3) |
| **APTT2** | 9 samples | 3.0 (2.7-3.4) | 2.2 (2.0-2.5) | 4.5 (3.4-6.8) | 4.6 (3.5-6.8) |
| 12 samples | 3.2 (2.9-3.5) | 2.7 (2.5-3.0) | 4.5 (3.4-6.7) | 4.5 (3.4-6.7) |
| **PT1** | 9 samples | 7.6 (6.9-8.6) | 2.6 (2.3-3.0) | 5.8 (4.1-9.1) | 6.0 (5.0-9.8) |
| 12 samples | 7.2 (6.5-7.9) | 3.4 (3.0-3.7) | 5.6 (4.1-8.7) | 6.1 (4.7-9.3) |
| **PT2** | 9 samples | 2.4 (2.2-2.8) | 2.2 (2.0-2.5) | 4.7 (3.5-6.8) | 4.7 (3.5-6.9) |
| 12 samples | 3.4 (3.1-3.7) | 2.6 (2.4-2.9) | 4.5 (3.3-6.6) | 4.6 (3.4-6.7) |
| **INR1** | 9 samples | 7.0 (6.2-7.9) | 2.3 (2.1-2.7) | 4.7 (3.2-7.4) | 5.5 (4.2-8.2) |
| 12 samples | 6.5 (6.0-7.2) | 3.0 (2.7-3.4) | 4.5 (3.3-7.0) | 5.1 (3.9-7.6) |
| **INR2** | 9 samples | 2.5 (2.3-2.9) | 2.3 (2.1-2.6) | 4.8 (3.5-7.0) | 4.8 (3.6-7.0) |
| 12 samples | 3.5 (3.2-3.8) | 2.7 (2.4-3.0) | 4.6 (3.4-6.7) | 4.7 (3.5-6.8) |
| **Fibrinogen** | 9 samples | 14.0 (12.6-15.9) | 7.2 (6.4-8.1) | 12.6 (9.2-19.4) | 13.8 (10.5-20.7) |
| 12 samples | 18.1 (16.5-20.1) | 8.9 (8.0-9.8) | 12.0 (8.5-18.6) | 13.5 (10.1-20.1) |
| **Factor VIII** | 9 samples | 32.4 (29.1-36.6) | 12.2 (10.9-13.9) | 16.9 (10.2-27.1) | 18.6 (13.8-27.9) |
| 12 samples | 35.2 (32.1-39.0) | 12.7 (11.6-14.2) | 16.0 (9.9-25.8) | 18.2 (13.6-27.2) |
| **vWF:antigen** | 9 samples | 34.9 (31.3-39.3) | 11.3 (10.1-12.8) | 25.0 (17.5-39.1) | 28.6 (21.8-43.7) |
| 12 samples | 44.9 (41.0-49.7) | 13.7 (12.5-15.2) | 21.5 (13.9-34.7) | 26.5 (20.0-40.1) |
| **Non-pregnant** |  | **CVI % (95%CI)** | **CVI % (95%CI)** | **CVG % (95%CI)** | **CVG % (95%CI)** |
| **APTT1** | 10 samples | 2.8 (2.5-3.2) | 2.7 (2.4-3.0) | 7.7 (5.6-11.4) | 7.6 (5.6-11.3) |
| **APTT2** | 10 samples | 2.1 (1.8-2.4) | 2.1 (1.8-2.3) | 5.8 (4.2-8.5) | 5.9 (4.2-8.5) |
| **PT1** | 10 samples | 3.4 (3.0-3.8) | 3.3 (2.9-3.7) | 7.5 (5.8-11.5) | 7.4 (5.8-11.4) |
| **PT2** | 10 samples | 2.5 (2.2-2.8) | 2.5 (2.3-2.8) | 2.9 (2.3-4.7) | 2.8 (2.2-4.5) |
| **INR1** | 10 samples | 3.0 (2.7-3.4) | 3.0 (2.7-3.4) | 7.3 (5.6-11.1) | 7.2 (5.5-10.9) |
| **INR2** | 10 samples | 2.5 (2.2-2.8) | 2.5 (2.3-2.9) | 2.9 (2.4-4.9) | 2.9 (2.3-4.7) |
| **Fibrinogen** | 10 samples | 9.7 (8.7-10.9) | 9.3 (8.3-10.5) | 19.0 (14.1-28.1) | 17.1 (12.8-25.9) |
| **Factor VIII** | 10 samples | 12.5 (11.2-14.1) | 11.7 (10.4-13.2) | 30.0 (21.8-43.4) | 31.4 (22.6-46.5) |
| **vWF:antigen** | 10 samples | 11.6 (10.4-13.2) | 11.1 (9.9-12.6) | 33.3 (24.1-49.6) | 31.6 (22.6-48.6) |

APTT, activated partial thromboplastin time, PT, prothrombin time, INR, International Normalized Ratio, FVIII:C, Factor VIII clot, vWF:ag, von Willebrand factor antigen.

**Supplemental Table 6.** Within- (CVI) and between- (CVG) subject biological variation (lnMoM)for pregnant women when all samples in pregnancy were included (all) and after sample exclusions (see materials and methods). CVI and CVG are given both for 9 samples (only pregnancy) and 12 samples (pregnancy and post-partum).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Based on lnMoM values for coagulation tests in pregnant women** | | | |
| **Parameter** | **CVI % (95%CI)**  **9 samples** | **CVI % (95%CI)**  **12 samples** | **CVG % (95%CI)**  **9 samples** | **CVG % (95%CI)**  **12 samples** |
| **APTT** (all)**a** | 3.0 (2.7-3.4) | 3.8 (3.5-4.2) | 5.3 (4.0-7.9) | 4.9 (3.7-7.3) |
| **PT1** (after exclusion) | 2.6 (2.3-3.0) | 3.4 (3.0-3.7) | 6.0 (5.0-9.8) | 6.1 (4.7-9.2) |
| **PT1** (all) | 2.9 (2.5-3.2) | 3.5 (3.2-3.9) | 6.9 (5.2-10.2) | 6.4 (4.5-9.5) |
| **PT2** (after exclusion) | 2.2 (2.0-2.5) | 2.6 (2.4-2.9) | 4.7 (3.5-6.9) | 4.6 (3.4-6.7) |
| **PT2** (all) | 2.5 (2.2-2.8) | 2.8 (2.5-3.1) | 4.7 (3.5-6.9) | 4.6 (3.4-6.7) |
| **INR1** (after exclusion) | 2.3 (2.1-2.7) | 3.0 (2.7-3.4) | 5.5 (4.2-8.2) | 5.1 (3.9-7.6) |
| **INR1** (all) | 3.2 (2.9-3.5)\* | 3.2 (2.9-3.5) | 5.8 (4.4-8.5) | 5.3 (4.0-7.9) |
| **INR2** (after exclusion) | 2.3 (2.1-2.6) | 2.7 (2.4-3.0) | 4.8 (3.6-7.0) | 4.7 (3.5-6.8) |
| **INR2** (all) | 2.6 (2.3-2.9) | 2.9 (2.6-3.2) | 4.8 (3.6-7.0) | 4.7 (3.5-6.8) |
| **Fibrinogen** (after exclusion) | 7.2 (6.4-8.1) | 8.9 (8.0-9.8) | 13.8 (10.5-20.7) | 13.5 (10.1-20.1) |
| **Fibrinogen** (all) | 16.1 (14.5-18.2)\* | 19.3 (17.6-21.4)\* | 11.7 (8.1-18.2) | 11.4 (7.8-21.4) |
| **FVIII:C** (after exclusion) | 12.2 (10.9-13.9) | 12.7 (11.6-14.2) | 18.6 (13.8-27.9) | 18.2 (13.6-27.2) |
| **FVIII:C** (all) | 13.4 (12.0-15.2) | 13.6 (12.3-15.1) | 18.5 (13.7-27.9) | 18.1 (13.5-27.2) |
| **vWF:Ag** (after exclusion) | 11.3 (10.1-12.8) | 13.7 (12.5-15.2) | 28.6 (21.8-43.7) | 26.5 (20.0-40.1) |
| **vWF:Ag** (all) | 12.2 (10.9-13.8) | 14.3 (13.0-15.9) | 28.7 (21.8-44.0) | 26.5 (20.140.3) |

\*Statistical significant different p<0.05. aNo outliers for APTT.

APTT, activated partial thromboplastin time, PT, prothrombin time, INR, International Normalized Ratio, FVIII:C, Factor VIII clot, vWF:ag, von Willebrand factor antigen.

**Supplemental Table 7.** Example of how to calculate the lnMoM fibrinogen change in a pregnant woman and

compare it to the lnMoM RCV SD for fibrinogen found in healthy pregnant women.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Fibrinogen (g/L)** | **MoM Fibrinogen** | **lnMoM Fibrinogen** |
| **Week 36 (healthy state)** | 4.6 | 4.6/4.4a = 1.05 | 0.05 |
| **Week 39 (suspected DIC)** | 3.6 | 3.6/4.5a = 0.8 | -0.22 |
| **Decrease in lnMoM Antithrombin from week 36 to 39** | | | -0.22 - 0.05 = -0.27b |
| **lnMoM RCV SD (unidirectional) for fibrinogen** | | | -0.18 |

aThe measured fibrinogen is divided by the median for the corresponding gestational period (Table 1; week 33-37, median 4.4 g/L

and week 37-40, median 4.5 g/L).

bTo be sure that a significant decrease has occurred from fibrinogen lnMoM 0.05, the next fibrinogen lnMoM value has to be

lower than 0.05 – 0.18 = -0.13, where -0.18 is the lnMoM RCV SD for fibrinogen in pregnancy (Table 2).

So the decrease of – 0.27 is considered significant.