**Supplementary File S4. Internal Quality Control (IQC) Program**

**S4.0. Scope and platforms**

- **Serum biochemistry panel:** performed in the study laboratory; analyzer **BS-200E (Mindray)** with **Spinreact** and **BioSystems** reagents.
- **Hormonal panel (TSH, FT3, FT4, insulin, cortisol):** performed at **Laboratorio Juan Bta. Montoro, S.L.**, accredited **ISO 15189** and certified **ISO 9001**, using **ADVIA Centaur® XP/XPT (Siemens Healthineers)**.
- The following are presented: (i) **internal controls** from the study laboratory (S4.2), (ii) **internal verification** at Montoro (S4.3), and (iii) **manufacturer's declared precision (CV%)** from the package inserts (S4.4 and S4.5).

**S4.1. Control materials and calibrators (according to IFU provided)**

**Spinreact (Glucose, Total cholesterol, HDL-c D, Urea, ALP, Magnesium, Total bilirubin, CRP-turbilatex, Uric acid)**

- Controls: *SPINTROL H Normal and Pathological*.
- Calibrators: GLUCOSE CAL, CHOLESTEROL CAL, HDLc/LDLc CAL, UREA CAL, MAGNESIUM CAL, Bilirubin CAL, CRP-CAL, URIC ACID CAL.

**BioSystems (Triglycerides, γ-GT)**

- Controls: *Biochemistry Control Serums* (Levels I and II).
- Calibrators: Triglycerides standard (glycerol equivalent to triolein 200 mg/dL).

**Siemens (hormones, ADVIA Centaur XP/XPT)**

- Recommended internal controls: Siemens controls, two levels, at least once daily and after each calibration or reagent lot change, as specified in the IFU.

**S4.2. Serum biochemistry panel — Internal controls of the study laboratory (BS-200E)**

**Table S4-A. Repeatability (intra-series) and intermediate precision (inter-series)**
*(n = replicates; values and units as in the control files.)*

| Analyte | n Inter | Mean Inter (SD) | CV% Inter | n Intra | Mean Intra (SD) | CV% Intra |
|---|---|---|---|---|---|---|
| Albumin | 15 | 3.58 (0.07) | 2.01 | 15 | 4.27 (0.04) | 0.91 |
| Total bilirubin | 15 | 0.90 (0.07) | 7.51 | 15 | 0.44 (0.05) | 11.76 |
| Creatinine | 15 | 1.22 (0.07) | 5.55 | 15 | 1.49 (0.04) | 2.56 |
| Total cholesterol | 15 | 95.27 (1.71) | 1.79 | 15 | 185.60 (7.49) | 4.04 |
| HDL-cholesterol | 15 | 34.60 (4.72) | 13.64 | 15 | 79.13 (2.03) | 2.57 |
| Urea | 15 | 37.20 (1.61) | 4.33 | 15 | 34.20 (0.86) | 2.52 |
| Uric acid | 15 | 4.56 (0.15) | 3.19 | 15 | 7.37 (0.08) | 1.08 |
| Triglycerides | 15 | 115.60 (1.72) | 1.49 | 15 | 80.53 (1.60) | 1.98 |
| CRP (standard, not hs-CRP) | 15 | 7.25 (0.25) | 3.41 | 15 | 0.69 (0.16) | 22.78 |
| Alkaline phosphatase | 15 | 190.20 (10.67) | 5.61 | 15 | 198.13 (9.07) | 4.58 |
| Glucose | 15 | 108.20 (2.62) | 2.43 | 15 | 96.47 (1.81) | 1.87 |
| Magnesium | 15 | 19.01 (1.20) | 6.30 | 15 | 20.10 (0.49) | 2.44 |
| γ-GT | 15 | 36.80 (0.86) | 2.34 | 15 | 12.87 (0.35) | 2.73 |

**S4.3. Hormonal panel — Internal controls at Montoro Laboratory (ADVIA Centaur XP)**

**Source:** Excel "control de calidad interserie/intraserie e intervalo suero control.xlsx".
**Calculation:** Mean, sample SD (n−1) and CV%. n=10 replicates per condition.
**Control intervals (IFU):** Insulin 44.8–71.6 mU/L; Cortisol 12.1–21.8 µg/dL; TSH 5.08–7.98 mIU/L; FT3 5.67–7.28 pg/mL; FT4 1.76–2.86 ng/dL.

**Table S4-H1. Repeatability (intra-series) and intermediate precision (inter-series)**

| Analyte (units) | Intra — Mean (SD) | CV% Intra | Inter — Mean (SD) | CV% Inter | Control interval |
|---|---|---|---|---|---|
| Insulin (mU/L) | 66.03 (0.71) | 1.07 | 65.96 (0.79) | 1.19 | 44.8–71.6 |
| Cortisol (µg/dL) | 18.38 (0.52) | 2.81 | 18.01 (0.46) | 2.54 | 12.1–21.8 |
| TSH (mIU/L) | 5.38 (0.13) | 2.45 | 5.44 (0.26) | 4.84 | 5.08–7.98 |
| FT3 (pg/mL) | 6.34 (0.03) | 0.54 | 6.32 (0.18) | 2.84 | 5.67–7.28 |
| FT4 (ng/dL) | 2.20 (0.04) | 1.90 | 2.27 (0.08) | 3.48 | 1.76–2.86 |

**S4.4. Serum biochemistry — Precision declared by the manufacturer (Spinreact, BioSystems IFU)**

**Table S4-B. Declared repeatability (intra) and reproducibility (inter).**

| Analyte (method) | Level ~mean | CV Intra | n | CV Inter | n |
|---|---|---|---|---|---|
| Glucose-LQ (Spinreact) | 98.5 mg/dL | 0.59% | 20 | 2.97% | 20 |
| | 264.8 mg/dL | 0.48% | 20 | 2.57% | 20 |
| Total cholesterol-LQ (Spinreact) | 99 mg/dL | 0.84% | 20 | 1.82% | 20 |
| | 201 mg/dL | 0.70% | 20 | 3.26% | 20 |
| HDL-c D (Spinreact) | 28.0 mg/dL | 0.89% | 20 | 4.60% | 20 |
| | 76.1 mg/dL | 1.06% | 20 | 2.71% | 20 |
| Triglycerides (BioSystems) | 100 mg/dL | 1.7% | 20 | 2.6% | 25 |
| | 245 mg/dL | 0.7% | 20 | 1.2% | 25 |
| γ-GT (BioSystems) | 31 U/L | 1.6% | 20 | 4.8% | 25 |
| | 99 U/L | 0.5% | 20 | 1.4% | 25 |

| Analyte (method) | Level ~mean | CV Intra | n | CV Inter | n |
|---|---|---|---|---|---|
| Alkaline phosphatase (Spinreact) | 174 U/L | 0.41% | 20 | 3.93% | 20 |
| | 443 U/L | 0.35% | 20 | 2.75% | 20 |
| Total bilirubin (Spinreact) | 1.53 mg/dL | 1.73% | 20 | 1.92% | 20 |
| | 5.06 mg/dL | 1.01% | 20 | 2.18% | 20 |
| Urea-LQ (Spinreact) | 37.5 mg/dL | 2.79% | 20 | 2.65% | 20 |
| | 120 mg/dL | 0.77% | 20 | 1.65% | 20 |
| Magnesium (Spinreact) | 2.39 mg/dL | 1.18% | 20 | 2.99% | 20 |
| | 4.01 mg/dL | 1.73% | 20 | 3.22% | 20 |
| CRP-Turbilatex (Spinreact) | 8.6 mg/L | 6.5% | 10 | 7.7% | 10 |
| | 16.8 mg/L | 3.6% | 10 | 6.6% | 10 |
| | 50.5 mg/L | 1.9% | 10 | 6.3% | 10 |
| Uric acid-LQ (Spinreact) | 4.46 mg/dL | 0.46% | 20 | — | — |
| | 4.71 mg/dL | — | — | 1.37% | 20 |

**S4.5. Hormonal panel — Precision declared by the manufacturer (Siemens, ADVIA Centaur XP/XPT IFU)**

**Table S4-C. Manufacturer's declared precision (CV%) from Siemens IFU**

| Assay (Siemens) | Level ~mean | CV Intra | CV Total/Inter | n | IFU source |
|---|---|---|---|---|---|
| TSH3-Ultra II | 0.5–98 mIU/L | 1.7–2.5% | 2.6–4.0% | 80 | IFU TSH3-Ultra II |
| FT3 | 2.7–14.8 pg/mL | 1.3–2.7% | 2.0–3.7% | 80 | IFU FT3 |
| FT4 | 0.3–6.0 ng/dL | 2.2–3.3% | ≤8% | 80 | IFU FT4 |
| Insulin | 14–125 mU/L | 3.2–4.6% | ≤11% | 80 | IFU Insulin |
| Cortisol | 2.8–50 µg/dL | 2.9–4.2% | 4.4–6.0% | 80 | IFU Cortisol |