RESULTS OF THE MASTER LOT CALIBRATION OF A NEW COAGULATION MONITORING SYSTEM FOR PATIENT SELF TESTING

Ingrid Leichsenring[1], Winfried Plesch[1], Volker Unkrig[1], Alex Newhart[1], Steve Kitchen[2], Dyanne P Kitchen[2], Rhona Mclean[2], Bert Dikkeschei[3], Ton van den Besselaar[4]

[1]Roche Diagnostics, Mannheim, Germany, and Indianapolis, USA; [2]Royal Hallamshire Hospital, Sheffield, UK; [3]Isala Klinieken, Zwolle, The Netherlands; [4]Leiden University Medical Centre, Leiden, The Netherlands

BACKGROUND

The new CoaguChek® XS system is designed for use in patient self testing. It will be the successor of the current CoaguChek® S system. The detection principle is based on the amperometric measurement of the thrombin activity initiated by starting the coagulation cascade using a human recombinant thromboplastin. This study was performed to assign the ISI to the new test according to the WHO guidelines for thromboplastins and plasmas used to control anticoagulant therapy.

MATERIALS AND METHODS

At four sites a total of 90 samples of normal donors and 291 samples of warfarin, phenprocoumon or acenocoumarol treated patients were included in the study. Non citrated venous whole blood was applied to the master lot test strips of the new system in duplicate. Raw PT clotting times were read from the display. From the same venipuncture corresponding plasma samples were collected into Vacutainer tubes (105 mM citrate). PT results were obtained using the international reference preparations (IRPs) rTF/95 and CRM149S by the manual tilt tube method. 14 samples of donors under oral anticoagulation had to be omitted from the analysis as outliers or due to missing data. After eliminating another 12 samples from the analysis due to poor stabilization of anticoagulation (INR > 4.5) the ISI values of the new test were assigned against the human recombinant reference thromboplastin rTF/95 at each site according to the procedure given in the WHO guidelines. In ISI assignment 2 outliers with deviations > 3 SD from the regression line were detected and not included in the analysis (Indianapolis 1, Sheffield 1).

RESULTS

The results of the ISI assignment are summarized in Table 1 (Fig. 1 to 4).

Table 1: ISI assignment of the CoaguChek XS PT master lot

Site	ISI	slope CV	n (normals / patients)
Indianapolis	0.99	1.1%	91 (22 / 69)
Mannheim	1.02	2.0%	85 (23 / 62)
Zwolle	1.03	1.1%	88 (22 / 66)
Sheffield	1.00	1.4%	89 (23 / 66)

All regression lines calculated from patient data pass through the normal donor data points. All CVs of the slopes of the orthogonal regression lines are well below 3% thus fulfilling the requirements of the WHO guidelines.

The mean ISI for the new CoaguChek® XS PT Test is 1.01.

Additionally a polynomial regression curve was calculated to calibrate the new test versus the mean INR of the two international reference preparations. These data are transformed to support points giving the relationship between raw clotting times of the new test and corresponding INR values. The support points will be stored in a code chip coming with each vial of test strips.

For the CoaguChek® XS master lot this procedure was double-checked by converting the raw PT clotting times by means of the polynomial curve to INR and performing a method comparison versus the mean INR values of the IRPs.
The regression line after Bablok-Passing was y = 0.996x - 0.001 (x: mean IRP), the mean bias for patient data only was -0.01 INR or - 0.04% (Fig. 5 and 6).
The duplicate determinations with the CoaguChek® XS system showed a very low imprecision (high precision) for the master lot INR results with a CV of 1.1% (Fig. 7).

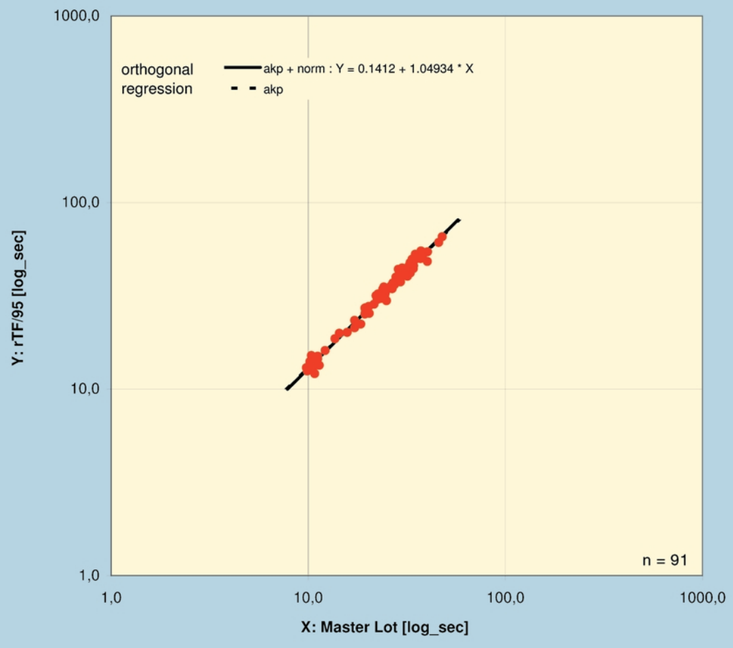

Fig. 1: ISI assignment of the CoaguChek® XS master lot (Indianapolis)

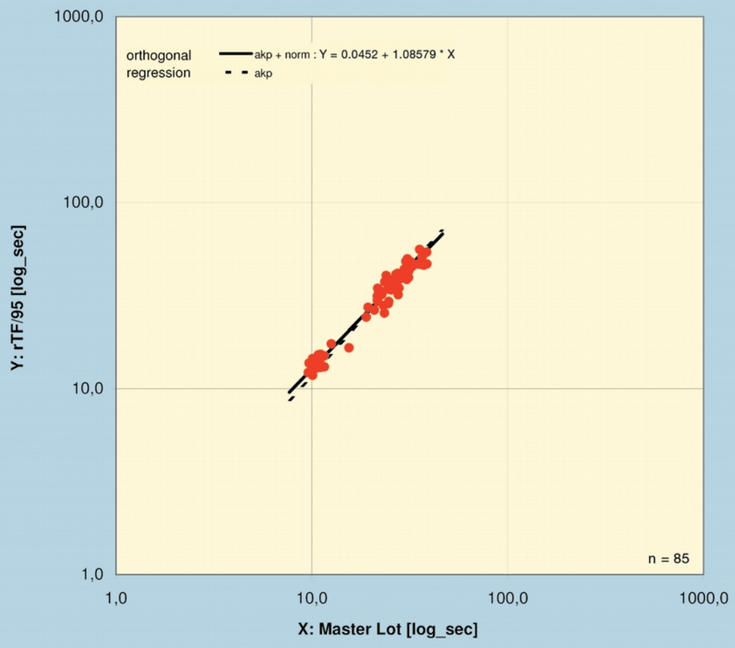

Fig. 2: ISI assignment of the CoaguChek® XS master lot (Mannheim)

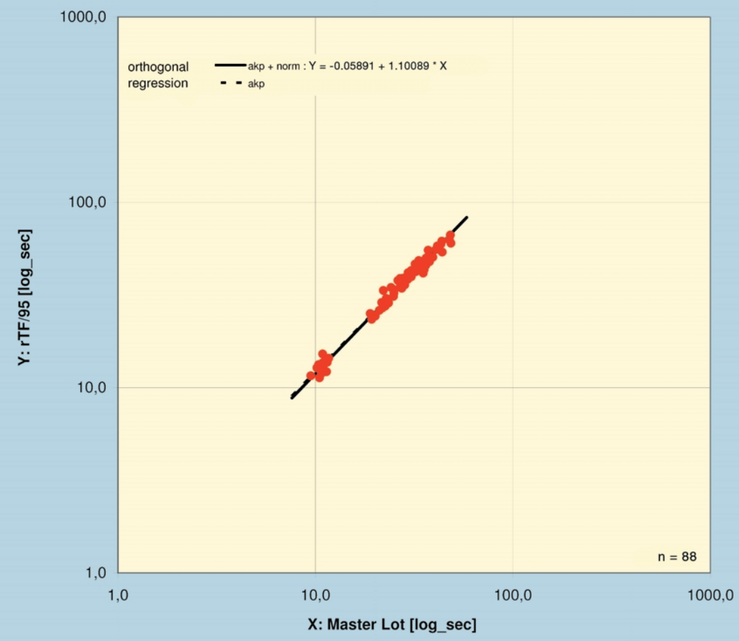

Fig. 3: ISI assignment of the CoaguChek® XS master lot (Zwolle)

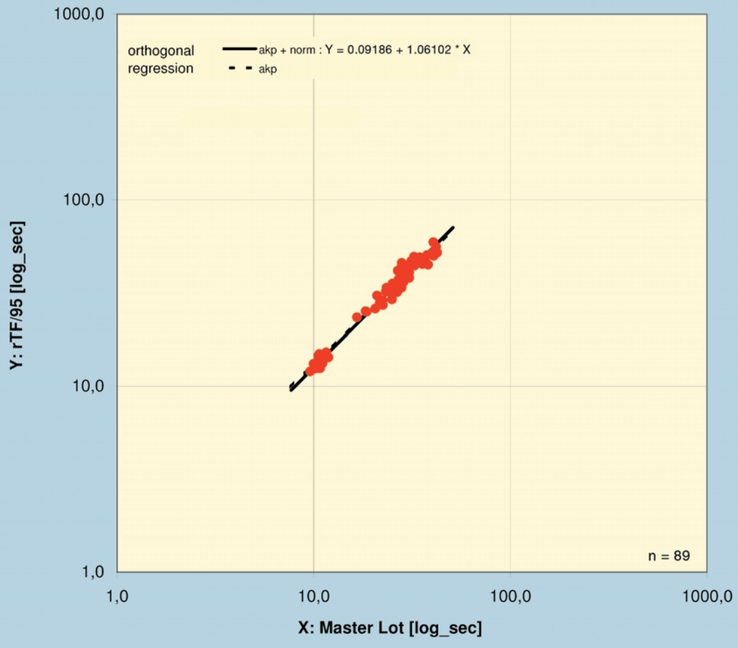

Fig. 4: ISI assignment of the CoaguChek® XS master lot (Sheffield)

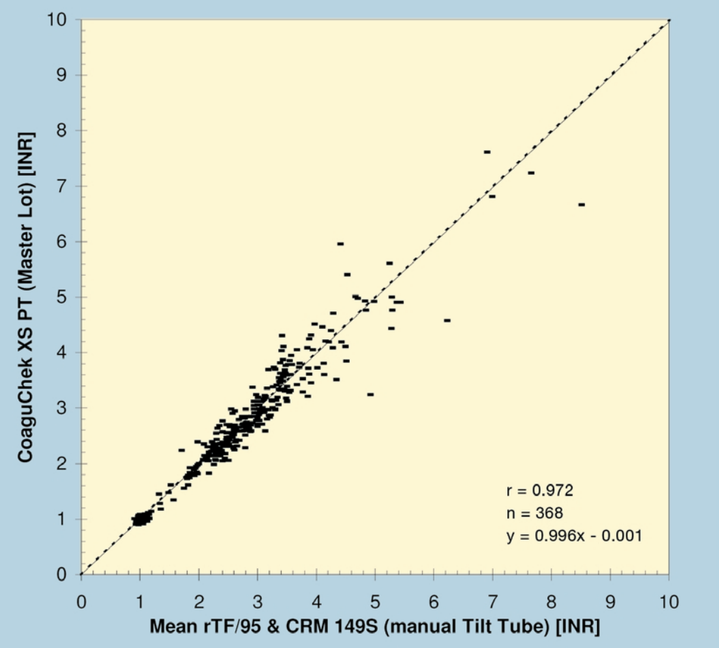

Fig. 5: Method comparison of the CoaguChek® XS master lot versus mean IRP (scatter plot)

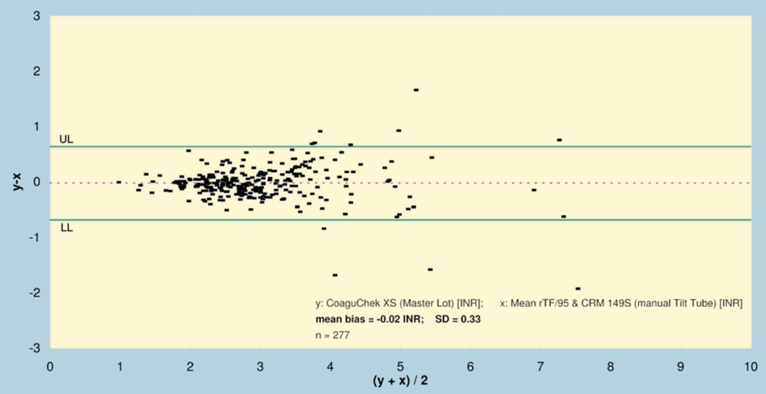

Fig. 6: Method comparison of the CoaguChek® XS master lot versus mean IRP (Bland-Altman plot, * LL = Lower Limit of agreement, UL = Upper Limit of agreement)

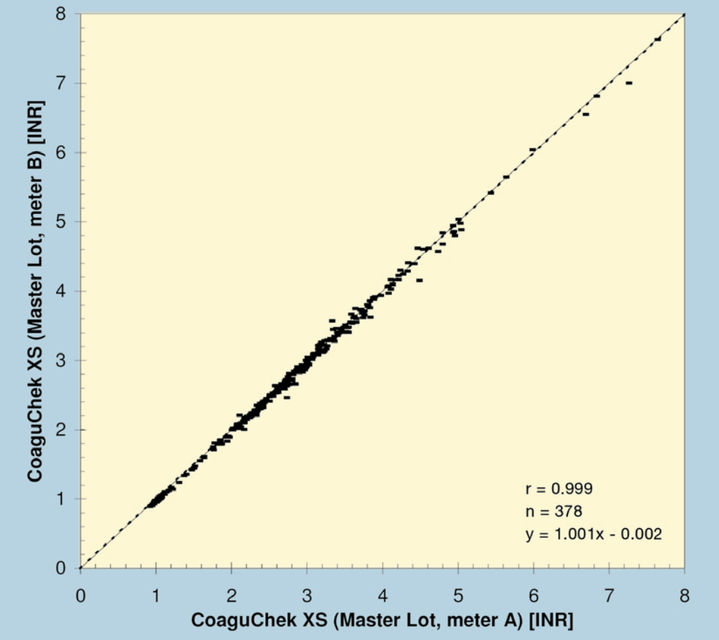

Fig. 7: Method comparison of duplicate determinations with the CoaguChek® XS master lot

CONCLUSION

The master lot of the new CoaguChek® XS system was successfully calibrated with high precision according to the WHO guidelines.

Poster presented at the XX[th] ISTH Congress 2005, Sydney, Australia