Memo

Roche

To whom it may concern

This document serves to inform you about the definition of control ranges established on all Elecsys systems (**cobas e** 411, **MODULAR** *ANALYTICS* <E>, **cobas e** 601, **cobas e** 602 and **cobas e** 801) for PreciControls of quantitative and qualitative Elecsys assays.

The materials and protocols employed at Roche in order to determine the analyte value and the 3 SD-ranges for their PreciControls ensure that the reagent standardization are correct according to the intended use for human serum and no variation on patient samples are expected with new reagent lots in comparison to former reagent lots.

Roche control materials are intended to monitor reliability of a test system and help minimize reporting of incorrect test results. Roche undertakes great efforts that QC materials simulate the composition of patient samples as closely as possible in order to minimize matrix effects and correctly reflect the expected performance with patient samples. However, e.g. lyophilisation or inactivation may significantly alter the physical, chemical, or biological properties of the QC material and together with preparatory steps required for the assay (i.e. dilution of lyophilisates), these deviations from human samples may impair the QC material's ability to reflect performance of the assay for 'natural' human samples.

The control ranges stated for Elecsys assays on the corresponding value sheet corresponds to ± 3 SD ('SD' = one third of the confidence range). In this context the 'SD' is not a statistical figure but describes an interval where the measured result of the control could reasonably be expected. Hence, this control range ('SD') is not to be mistaken for the typical precision as stated in the package insert. Within the control ranges normal random (e.g. within-run, run-to-run) and systematic variations (system-to-system, lot-to-lot, stability etc.) as well as reagent aging, matrix variations of the control material relative to human samples are accommodated in order to avoid

Roche Diagnostics GmbH; Werk Penzberg; Nonnenwald 2; D 82377 Penzberg; Telefon +49 8856 60 0; Telefax +49 8856 60 3896

unnecessary false alarms. In addition, the trade-off between complexity of lot specific control target values and accuracy of target value recovery contributes to the claimed control range.

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Sincerely,

Dr.Ursula Giesen
Head of Case Investigation &
Resolution HetIA Application

Dr. Anja Ruschel-Mitscherlich
Head of Standardization and Quality
Control