Establishing reference values - with low number of control samples –

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At the ECAT meeting 2012, professor Horowitz (Harvard Medical School, USA) presented a practical approach to establishing reference intervals based on the recommendation of the CLSI (Clinical and Laboratory Standards Institute). According the CLSI C28-A3c (Defining, establishing, verifying reference intervals in the clinical laboratory, 2010, third edition) reference limits should be preferably determined by the nonparametric method with a lower and upper CI (Confidence Interval) of 90%. This implies a minimum size of 120 control samples. However, in daily clinical practice it is often difficult to obtain appropriate reference subjects in sufficient number. In this case, the CLSI guideline recommends to use a parametric or robust method. The CLSI guideline postulates that the robust method may offer the best way to deal with low number of samples because, in contradiction to the parametric method, the population of analytical data does not need to follow a Gaussian distribution.
In this presentation results are shown of the nonparametric, parametric and robust method for establishing reference intervals for the coagulation screenings tests: APTT, PT and fibrinogen. Data sets from 20-120 control samples from the Rijnstate Hospital (Arnhem, The Netherlands) were analyzed with two clinical laboratory software programs: EP Evaluator **(**http://www.datainnovations.com**)** and Reference Value Advisor **(**http://www.biostat.envt.fr/spip/spip.php?article63**).** Results of the reference and confidence intervals, based on 120 control samples and determined with the nonparametric, parametric and robust method, will be compared with regard to the width of the reference and confidence intervals, and previous published data. Based on the results of the reference and confidence intervals determined with the parametric and robust method to less than 120 control samples, an example of the possibilities and limitations of these methods is given.