

Afssaps market surveillance 2005-2006 of instruction for use for cortisol in vitro diagnostic medical devices

Cortisol (hydrocortisone or compound F) is the principal and most abundant glucocorticoid hormone. The determination of circulating blood cortisol level is useful for screening or diagnosis in conditions of hypo- or hypercorticism. The measurement of cortisol in other biological type of sample, in particular urine, can be an important factor in the diagnosis of Cushing's syndrome and the search for its causes. As one of its assignments, Afssaps has set up a market surveillance of the instructions for use (IFU) of cortisol test systems. This market surveillance consists of checking that all the indications imposed by the essential requirements of european directive 98/79/CE relating to in vitro diagnostic medical devices were well presented in the IFU. In addition, this market surveillance enabled the study, in collaboration with two expert biologists, of the different methods described for each of the 23 devices on the market according to the type of sampling advised.

Examining the devices shows that for the 23 devices on the market, 22 permit the measurement of cortisol in serum and/or plasma and only one is specifically devoted to salivary measurement. Among these 22 devices, 15 propose urinary measurement and 3 of salivary measurement. Out of 15 urinary assays, 11 recommend a preanalytical extraction phase which is optional. The analysis of the IFU made it possible to highlight major differences in the evaluation of the devices depending on the manufacturers, in particular in terms of accuracy and according to the type of sampling. The materials and reference methods currently recognized for the serum should permit harmonization for achieving accuracy of serum results. The differences observed between the devices offering urinary assays can doubtlessly be explained by the fact that the preanalytical phase is not systematically offered and also by the lack of material or reference methods. Moreover, in comparison with the essential requirements of directive 98/79/CE, the IFU showed certain nonconformities, in particular the absence of any mention of measurement range.

Afssaps which took up these nonconformity issues and observations with the manufacturers concerned continues to monitor the manufacturers. In order to harmonize the results of various measurement of Cortisol (current and forthcoming), Afssaps and the group of experts have decided to disseminate some recommendations :

- Accuracy (trueness) : the device must be correlated with the reference method, i.e. mass spectrometry coupled with gas chromatography. The concentrations of the samples chosen to undertake a correlation study should cover the whole of the measurement range. The expected bias of the device with the reference method should be indicated in the IFU. The results should be validated by the measurement of recognized reference materials already validated for the different kinds of sampling in question.

- Measurement range : the lower end of the suitable measurement range is, at the minimum, the limit of functional detection. If the manufacturer wishes to choose a lower concentration, the expected accuracy (variation coefficient) at this concentration will have to be mentioned.

- Relevant interferences : Prednisolone, prednisone, corticosterone, cortisone, 1 desoxycortisol, 21-desoxycortisol, tetrahydrocortisol, tetrahydrocortisone, 6 methylprednisolone, 17-hydroxyprogesterone

- Urine samples : the preliminary extraction of a urine sample avoids interferences related to steroids present in urine. The supplier should propose an extraction protocol as well as an evaluation tool for of the quality of the extraction. The advantage of a preanalytical extraction phase should be clarified in the IFU.