Afssaps market survey of total PSA, free PSA and complexed PSA assay kits

AFSSAPS

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In view of the clinical impact of prostate-specific antigen (PSA) assays for prostate cancer screening, Afssaps has conducted, in the context of its mission, a market survey of devices indicating quantitative results. The objective of this survey was to evaluate the analytical performances of these assays, particularly to verify the accuracy of total PSA, free PSA and complexed PSA assay kits and to study the equimolarity of total PSA reagents in the analogous recognition of the various forms of serum PSA (free PSA/bound PSA) by measuring 2 ng/ml, 4 ng/ml and 10 ng/ml samples of total PSA containing 0%, 25%, 50%, 75% or 100% of free PSA, prepared from Stanford University standard solutions (Stamey). Package leaflets were also examined to verify compliance with the essential requirements defined in Directive 98/79/EC.

The 37 assay kits available on the market (19 total PSA assay kits, 1 kit combining total PSA and free PSA assay, 15 free PSA assay kits and 2 complexed PSA assay kits) were evaluated according to a protocol prepared and validated by a working party and sent to the manufacturers prior to inspection. Analysis of the results of the technical evaluation showed that 7 total PSA assay kits gave results considered to be acceptable by the working party in terms of accuracy. Similarly, 9 total PSA assay kits showed equimolar characteristics. Nine free PSA or complexed PSA assay kits gave satisfactory results in terms of accuracy. Various non-conformities with Directive 98/79/EC were observed in the package leaflets for the assay kits evaluated.

Letters reporting these results were sent to the manufacturers at the end of June 2005. Most manufacturers decided to perform control tests in view of the results sent to them. After these control test, some manufacturers have decided to re-standardize their assay kits, while others have decided to clearly indicate the existence of a bias in the package leaflet. Afssaps is continuing to provide support for some manufacturers.

In order to harmonize the results of the various assay kits (current and future), Afssaps and the working party would like to propose certain guidelines.

Accuracy :	accuracy of the assay must be evaluated by using the Stanford international standard (100% free PSA, 100% complexed PSA and 90/10 complexed PSA/free PSA) diluted in a non-serum matrix (for example PBS buf fer + 1% BSA)
Equimolarity :	clearly indicate in the package leaflet the molar ratios obtained at various total PSA concentrations. The molar ratio is determined by calculating the following ratio: total PSA value at 100% free PSA/total PSA value at 0% free PSA. Acceptable values for the molar ratio according to the experts of the working party Afssaps are between 85 and 115%. Equimolarity is defined by the capacity of the system (device) to recognize the free and bound forms in an identical way.
Free/total ratio :	the package leaflets for free PSA assay kits should indicate diagnostic sensitivity and specificity data for the free PSA/total PSA ratio, by specifying the total PSA assay kit used.