Response to Reviews for EDL Submission

Prostate Specific Antigen

Pre-submission ID Number: 62
Full Submission ID Number: 29

Reviewer’s questions in bold font

#Reviewer 1

1. **Provision of evidence on robustness of IVDs especially in tropical countries.**

ECLIA system for the measurement of PSA is calibrated at 20-25°C, at the moment of the assay. The reagents are stable at 2-8°C (refrigerated), till the data of expiration and for 12 weeks after opening the ampoules and 4-8 weeks in the analyser. PSA assay is currently used for the management of prostate cancer in African countries, including tropical areas. For instance, a series of patients has been reported from Nigeria (Yunusa B et al, Nigeria Journal of basic and clinical sciences, 2017), replicating the results and the interpretation of the available literature. The test is extensively used in several tropical countries, like Trinidad and Tobago (Persaud S et al, ecancermedicalscience 2018) and different Caribbean countries including The Bahamas and Barbados (Persaud S et al, ecancermedicalscience 2018 - 12:842), Jamaica (Condappa A et al, ecancermedicalscience 2018) and Guadeloupe (Brureau L et al, Proigrès en urologie, 2018).

2. **Information on EQA/PT (External Quality Assessment/Proficiency Testing studies).**

The performance of the ECLIA test (Cobas, Roche Diagnostics Corporation, Indianapolis) has been compared to the Hybritech PSA assays on the Beckman Coulter Access Chemiluminescent Immunoassay System (Fullerton, CA), an alternative ECLIA (Butch, A.W., Crary, D., Yee, M. (2001). Analytical performance of the Roche total and free PSA assays on the Elecsys 2010 immunoanalyzer. Clin. Biochem.; 35, 143-145). Within run, CVs were less than 5%, covering a wide range of values. For PSA, the assay was linear between 0.01 and 103 g/L, as indicated by a slope of 0.999. At a PSA mean value of
0.01g/L total imprecision was 13.6%, confirming the manufacturers stated functional sensitivity of 0.03g/L. The two methods reported similar performance; the Deming regression analysis yielded the following statistics for PSA: slope equal to 0.923 (SD=0.007); r=0.993; Sy/x=0.45.

#Reviewer 2

1. **FDA or Eurostar Approval?**

In 1986, the PSA test was first approved by the FDA for monitoring the progression of prostate cancer in men who had already been diagnosed; risk definition at diagnosis (e.g. D’Amico score) is comprised in this approved indication (Venkatachalam S, Prostate cancer. Chapter 64 - Health Policy for Prostate Cancer: PSA Screening as Case Study. Science and clinical practice, 2016). In 1994, the FDA also approved the use of the PSA test in conjunction with a digital rectal exam for screening and then rectified in the context of an informed early detection strategy in selected men, as part of a tailored strategy; however, this indication is not part of this submission as not a priority nor a recognized screening method per WHO and IARC. In Europe, the analyzer submitted meets the requirements stated in Directive 98/79/EC of the European Parliament and the Council of the European Union (EU) on in vitro diagnostic medical devices and the marked authorization for the kit is granted (Roche Diagnostics, manual of use).

2. **Anticipated number of cases at any center? Whether training facility available for training technical staff?**

The number of cases to maintain competency and optimize performance is to be determined locally. Training for PSA testing is part of the general laboratory diagnostics training, as included in the core curriculum for laboratory technician (mid-level health workers); despite the kit being specific for PSA, the technique of analysis is used for different indications and the principle is the same. The requirements under a functional quality management system in the laboratory are determined per accreditation schemes.