Reviewer’s Questionnaire for Evaluation of Submissions for EDL v3
Based on the Criteria for Selection of Essential Diagnostics for the EDL

Diagnostic test: Prostate specific antigen
Test purpose: As an aid in diagnosis, prognosis and surveillance for prostate cancer
ID number: PreSubmission_ID62_FullSubmission_ID29

The selection process for essential diagnostics for the EDL will include consideration of a number of factors, including:

1. The public health and clinical need for the category of tests as determined for example, by disease burden and whether the proposed category of IVDs can help to bridge any existing gap in access to diagnostics that has been identified.

Questions:
1. Does the disease addressed by the test cause:
   ☒ a high burden of morbidity (human suffering)
   ☒ mortality
   ☒ cost on the populations and societies where it occurs

2. How strong is the evidence provided to support this?
   ☐ weak
   ☒ strong

Please complete the sub-questions below on evidence provided:

   a. Disease prevalence data?
      ☒ yes
      ☐ no

   b. Information on the disease impact on the quality of life of its sufferers?
      ☒ yes
      ☐ no

   c. Information on the disease impact on the quality of life of the families of sufferers and the communities in which they live? E.g. patients with high care needs, orphans, spread of infection
      ☒ yes
      ☐ no

   d. Impact assessments on health care resources and budgets?
      ☐ yes
      ☒ no
      I don’t think that this information is available.

2. Is any information provided showing the degree of access to diagnostic testing for the addressed disease in the primary care setting?
   ☒ yes
   ☐ no
Comment:
Does the submitted test category help to increase access in any way? E.g. reduced skill required, lower cost, improved performance vs alternative options
NO. This is an additional test, so the cost cannot come down. But it will make it easier to determine recurrence of disease.
Note: Answers to the questions above will have been assessed as part of the screening application and will have been deemed acceptable. Nevertheless, information provided on these matters in the full application may be commented upon in your assessment.

2. **Availability of validated commercial diagnostic tests as indicated by sound and adequate data on quality, safety, performance, and regulatory status.**

Questions:

1. How many commercially available IVDs are included in the application for this category?
   - **ONE**
     a. Does the submission include a list?
        - ☐ yes
        - ☒ no
     Does the application consider IVDs of all technologies that are available for the analyte of interest?
        - ☐ yes
        - ☒ no
     There is one test. There are other manufacturers who likely have similar tests.

2. Which national regulatory bodies have approved these tests for market access e.g. CE IVD, US FDA, SFDA, WHO-PQ, others?
   - FDA

3. Have package inserts been provided showing studies demonstrating quality, safety, and performance of regulatory approved IVDs in this category? ONE.
   - Quality: ☒ yes ☐ no
   - Safety: ☒ yes ☐ no
   - Performance: ☒ yes ☐ no
     a. If so, what is your assessment of the strength of the study data described in the package inserts?

4. Have any independently published studies been provided, showing IVDs’ performances compared to a recognised gold standard? How strong are these studies?
   - ☐ yes ☐ no Other than the prostatectomy, there is no GOLD Standard!
     a. If no gold standard exists, what is your assessment of the characterisation of the studies’ specimens? Good.

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1 Technologies: It may be that, within the IVD category, there are tests that use different technologies to measure or detect the same analyte e.g. an RDT or and EIA for HIV antibody

2 Analyte: Marker that the IVDs in the category measures or detects
5. Where relevant, have studies to demonstrate ease of use by trained lay providers been provided? Needs well qualified and trained personnel!
  ☐ yes  ☐ no

What is your assessment of these studies?

6. Where relevant, have studies been provided to show the IVD’s robustness\(^3\) in variable environmental conditions e.g. temperature and humidity?
  ☒ yes  ☐ no

3. **Clinical effectiveness\(^4\)** based on published peer reviewed data, safety and comparative cost-effectiveness.

Questions:

1. Has the applicant provided strong peer reviewed clinical studies that demonstrate the clinical utility\(^5\) and effectiveness of IVDs in this category?
   - clinical utility:  ☒ yes  ☐ no
   - effectiveness:  ☐ yes  ☐ no  No good studies available. Some retrospective analyses, do give support to the use of tPSA data.

2. Are you satisfied that these studies are properly designed and sufficiently powered statistically to support their conclusions?
   - ☒ yes  ☐ no  *However, there are not enough powered studies to confirm efficacy. Though, it is most likely a good tool for prognostication and to determine tumor recurrence after a radical prostatectomy.*

3. Has the applicant provided cost effectiveness, health economics or budget impact studies demonstrating the value of IVDs in this category?
   - cost effectiveness:  ☐ yes  ☐ no  *There is no way to figure the cost effectiveness of the treatment.*
   - health economics:  ☐ yes  ☐ no
   - budget impact studies:  ☐ yes  ☐ no

   How strong are these studies in terms of design and statistical power?
   - ☐ weak
   - ☒ strong

4. Has the applicant provided pricing information for commercially available IVDs in this category?  ☒ yes  ☐ no
   a. Is the pricing information given inclusive of instrument and service costs where relevant?  ☒ yes  ☐ no
   b. In your experience, based on the pricing information provided, how accessible are IVDs in this category to LMIC settings?
      accessible:  ☐ yes  ☒ no

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\(^3\) Robustness: An IVD’s capacity to remain unaffected by small variations in method parameters, which provides an indication of its reliability during normal usage

\(^4\) Clinical effectiveness: The degree to which a particular health care intervention does more good than harm. It is measured by the number of lives saved, or by improvements of objective parameters of a morbid condition

\(^5\) Clinical utility: The likelihood of improved outcomes from use of diagnostic tests in the IVD category
4. **Appropriateness of the IVD category for use at specified levels of the laboratory or health care system.**

Answer questions 1 and 2 for each IVD technology in the category. A table may help with reaching your recommendation, the characteristics of each IVD represented by one row of the table.

a. What specimen type is required? Blood.

b. What skill level and training is required for specimen collection? E.g. Phlebotomist

   *A well trained health care worker-a trained medical laboratory technologist.*

c. Do specimens need to be processed in any way prior to analysis? E.g. centrifugation, microscope slide staining, etc.

   ☒ yes ☐ no

   i. If so, for how long and at what temperature is the specimen stable before being processed (00:00:00 hours, min, seconds format) 2—8 degrees C.

   ii. At what temperature is the processed specimen stored before testing (please specify if Celsius or Fahrenheit) 2-8 degrees C

d. How long does it take to get a result? E.g. can a result be obtained during a consultation i.e. < 10 minutes, or while the patient is at the facility i.e. 2 – 3 hours or specimens are tested in a batch using the IVD i.e. days?

   18 minutes, once the equipment is started.

e. Where relevant to the IVD has ease of and effective use by trained lay providers been demonstrated?

   ☒ yes ☐ no BUT Trained personnel!

f. What equipment, if any, is required to perform this type of test?

   An analyser, eg COBAS 601 or 602.

g. Do instruments need to be calibrated, maintained, or serviced on a regular basis?

   ☒ yes ☐ no

h. How robust is the IVD?

   Good. BUT all recommendations for QA and for QA samples must be followed.

i. What is the impact of an unreliable power supply, or can the IVD operate without a power supply?

   *I doubt that it could. All Labs should have a /would need a backup power system, since the reagents can be stored, they must be maintained at recommended*
temperatures.

What is the minimal skill level and training required for personnel to perform this test?
☐ Unskilled
☐ Skilled
☒ Highly trained

2. Considering a 4-tier laboratory system, with the following levels:
   i. Primary care
   ii. District hospitals/laboratories
   iii. Regional hospitals/laboratories and
   iv. National hospitals/Reference laboratories

in your judgement, which level would be best suited to handle the required complexity of the relevant IVD? Please include your answer in the table based on the likely availability of the following at district, regional and national laboratory level:

National Hospital/Reference Laboratories.

a. Infrastructure requirements e.g. instrument size and complexity, biosafety requirements Adequate sized facility to house the Analyser. But a lab handling this equipment must handle all sorts of other tests and equipment.
b. Specimen types Blood, peripheral samples.
c. Testing volumes expected (sample throughput required). Uncertain. Test is based on a kit, so a single test can be run. Preferable to do the free PSA also and to be able to use the ratio of the two, when needed. Test can be done singly or in batches. Left over reagents can be stored for a few weeks. antibodies
d. Complexity of specimen handling e.g. biosafety level required, centrifugation or complex protocols: Does not need complex protocols. requiring highly skilled laboratory technicians. The sample itself will not be any more complex than the above one,
e. Availability of infrastructure for transporting specimens
f. Result turn-around times required
g. Reagent shipping, storage and operating conditions required
h. Where relevant, instrument operating conditions required
i. Required qualifications, training and skill levels needed for test performance and result interpretation e.g. non-laboratory personnel for a simple rapid test, trained laboratory technician to perform routine testing, medically trained personnel for result interpretation, Ph.D. level scientist required for highly complex and variable methodologies At Least High school followed by MLT technologist training
j. Quality management requirements based on complexity of facilities & support required to perform the test Regional/National /Reference Lab

Proposed answer table: Answers depend on the size of the country and the population.
5. What is your recommendation to SAGE IVD? Please summarise the key points you considered in reaching your conclusion.

This should be a required test. It is a good one for prognostication and for diagnosing recurrence, without need for CT or MRI. Points considered:

a. Prostate cancer is common
b. Prostate cancer needing treatment is somewhat less common.
c. Recurrence of prostate cancer is common, especially in the young.
d. Recurrence/metastatic lesions are extremely painful
e. Their diagnosis would be a lot easier with the tPSA results
f. tPSA is used in most larger institutions and is reliable

Prostate cancer is not rare, in fact it is quite common.
A good prognostication tool is N/A

6. Please list the items that require further clarification from the originator of this submission.

a. FDA or Eurostar Approval: Yes/No
b. Anticipated number of cases at any center?
c. Whether training facility available for training technical staff??