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

Diagnostic test: Basic panel with Immunohistochemical testing (IHC) for solid tumors
Test purpose: As an aid in the diagnosis, subclassification, prognosis and treatment of solid tumors with an emphasis on childhood cancer.
ID number: PreSubmission_ID63_FullSubmission_ID38

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

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. However, these tests are critical for accurate diagnosis of many soft tissue tumors of childhood as well as for adults. These are the basic tests needed. Most large institutions would use a much larger number/panel of these IHC tests. In a resource challenged situation, these would be a good place to start.
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?
   - 5
   a. Does the submission include a list?
      ☒ yes  ☐ no
   b. Does the application consider IVDs of all technologies \(^1\) that are available for the analyte \(^2\) of interest?
      ☒ yes  ☐ no

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

3. Have package inserts been provided showing studies demonstrating quality, safety, and performance of regulatory approved IVDs in this category?
   No. BUT these are well accepted and so the use of on slide controls (positive and negative is usually done):
   a. If so, what is your assessment of the strength of the study data described in the package inserts? Strongly recommend these IHC tests.

4. Have any independently published studies been provided, showing IVDs’ performances compared to a recognised gold standard? How strong are these studies?
   ☒ yes  ☐ no These tests are only one part of the diagnostic stains involved. But, they are widely accepted IHC.
   a. If no gold standard exists, what is your assessment of the characterisation of the studies’ specimens?

5. These tests are only one part of the diagnostic stains involved. But, they are widely accepted IHC.

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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
6. Where relevant, have studies to demonstrate ease of use by trained lay providers been provided?
☐ yes ☒ no. These tests must be performed by well trained and qualified as well as experienced Health Care Workers.

What is your assessment of these studies? Good, useful and reliable results, when performed with good controls.

7. Where relevant, have studies been provided to show the IVD’s robustness\(^3\) in variable environmental conditions e.g. temperature and humidity?
☒ yes ☐ no
Tests are good at ambient temperatures. The antibodies have to be kept frozen, till ready to use and then reconstituted.

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
2. Are you satisfied that these studies are properly designed and sufficiently powered statistically to support their conclusions?
☒ yes ☐ no
These are iHC tests which are done as one part of tumor analysis. Their results are reliable, since the positive and negative controls are meant to be placed on each test slide.
3. Has the applicant provided cost effectiveness, health economics or budget impact studies demonstrating the value of IVDs in this category? Not possible, since these are but one small group of tests to be performed.
cost effectiveness: □ yes □ no
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

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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.
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
   not accessible: ☐ yes ☐ no
   Please provide examples to support your conclusions.

5. In your experience, do you consider the cost of tests in this category (cost per test includes reagents, any amortised instrument capital expenditure and service contracts) to justify the clinical benefits. Please provide examples to support your conclusions.
   ☒ yes ☐ no
   Examples For correct and complete diagnosis of a tumor, these tests are essential and with the accurate Dx, they will guide the accurate treatment.

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? Tumor tissue
   b. What skill level and training is required for specimen collection? E.g. Phlebotomist
      A qualified, Medical Laboratory Technologist, with a few years experience.
   c. Do specimens need to be processed in any way prior to analysis? E.g. centrifugation, microscope slide staining, etc. ☒ yes ☐ no
      Formalin fixed and paraffin embedded.
      i. If so, for how long and at what temperature is the specimen stable before being processed (00:00:00 hours, min, seconds format), Room temperature, in formalin(10%, buffered).
      ii. At what temperature is the processed specimen stored before testing (please specify if Celsius or Fahrenheit) : Ambient or room temperature.
   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?
      It will take 2-4 hours to perform.
   e. Where relevant to the IVD has ease of and effective use by trained lay providers been demonstrated? Not Needed. They are safe and reliable.
      ☐ yes ☐ no
   f. What equipment, if any, is required to perform this type of test?
      Manual or Automated Stainer.
g. Do instruments need to be calibrated, maintained, or serviced on a regular basis?
  ☒ yes ☐ no

h. How robust is the IVD? Very!

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

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:

   a. Infrastructure requirements e.g. instrument size and complexity, biosafety requirements
   b. Specimen types
   c. Testing volumes expected (sample throughput required)
   d. Complexity of specimen handling e.g. biosafety level required, centrifugation or complex protocols requiring highly skilled laboratory technicians
   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
   j. Quality management requirements based on complexity of facilities & support required to perform the test

Proposed answer table:

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<th>Primary care</th>
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<th>Regional hospitals/lab</th>
<th>National hospitals/Reference lab</th>
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5. What is your recommendation to SAGE IVD? Please summarise the key points you considered in reaching your conclusion.

6. This test should be accepted.
   Need: so that a good, detailed and accurate tumor analysis can be made
   So that the patient gets the most appropriate Chemo and radiotherapy.
   The cost: these tests are reliable and reproducible not overly expensive.

7. Please list the items that require further clarification from the originator of this submission.
   None.