2nd Edition of the EDL

EDL secretariat
Department of Essential Medicines and Health Products
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Open Session, Second Meeting of the SAGE IVD, 18 March 2019
Inclusion Criteria for EDL 2nd Ed

Criteria:

• Primary care:  ➤ For patients at entry level care facilities
• Public health relevance: ➤ High burden diseases, affordable, quality
• Evidence based: ➤ Supported by WHO guidelines & manuals and + available evidence
• Free of conflict of interests
• Have regulatory approval
• Be available worldwide

Similar process to the EMLs but adapted for IVDs

Priority disease areas for the 2nd Ed of the EDL are: public health emergencies, AMR, NCD’s & NTD’s, Influenza, reproductive health and fungal disease
4 different process for 2nd EDL

1. CHANGES TO 1ST EDL

117 suggested changes submitted since publication (May 2018):
  - Based on feedback received from stakeholders
    Some typographical errors, omissions implemented in November 2018.
  - All others: public comment and the SAGE IVD consideration.

2. NEW SUBMISSIONS

32 submissions received
  - 13 are cancer specific

3. GENERAL LABORATORY TESTS

  - New division – Anatomical Pathology
  - New test categories
  - Expansion of test categories already in 1st EDL

4. THERAPEUTIC DRUG MONITORING

  - 11 were reviewed
    - 4 are proposed to be included
    - 3 to be discarded
    - 4 to be analyzed for further work
1. Changes to 1\textsuperscript{st} EDL

117 suggestions for changes were received after the release of the first edition of the EDL
2. Process for review of applications for inclusion in the EDL

- Application assessed by EDL Secretariat for completeness & circulated to WHO departments
- Successful candidates invited to make full submissions
- Submission assessed by experts selected by WHO
- Submission posted on WHO website for comment
- Expert reviews published on WHO website
- Assessment reports presented at SAGE IVD meeting
- SAGE IVD recommend inclusions & exclusions to WHO
- SAGE IVD recommendations presented to WHO DG
## Summary of information included in a submission to the EDL

### 1. Applicant’s information
- Name of WHO focal point
- Name/info of applicant organisation(s)
- Name/info of Institutions consulted or supporting the application

### 2. Disease or conditions addressed
- Type of disease to be addressed
- Evidence for public health relevance & necessity
- Application of IVD (i.e. diagnostic testing algorithm)
- Patient information (condition, morbidity, mortality life quality, economic impact)

### 3. IVD description
- Category of test
- Intended use, detection target and setting
- Specimen type and sample volume
- Performance of test
- End-user
- Access to IVD
- Bio-safety requirements

### 4. Evidence summary (as available)
- Diagnostic accuracy
- Summary of evaluation studies
- Proof of clinical evidence
- Summary of non-clinical data (appraisal of quality, performance, ease of use, summary of results) and relevant references

### 5. Societal impact information (as appropriate)
- Ethical issues
- Human rights issues
- Equity issues

### 6. Budget and resources
- Summary of data on comparative cost and cost-effectiveness
- Resources and budget impact on health care systems (specialised HR, training etc)
<table>
<thead>
<tr>
<th>Name of the organization</th>
<th>Diagnostic Test</th>
<th>Test Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>World Health Organization</td>
<td>Qualitative test for the detection and differentiation of genomic DNA from Chlamydia trachomatis (CT) and Neisseria gonorrhoeae</td>
<td>For the diagnosis or as an aid in the diagnosis of chlamydial and/or gonorrhoeal urogenital disease</td>
</tr>
<tr>
<td>Global Action Fund for Fungal Infections</td>
<td>Histoplasma antigen test</td>
<td>As an aid in the diagnosis of histoplasmosis</td>
</tr>
<tr>
<td>International Patient Organisation for Primary Immunodeficiencies (IPOPI)</td>
<td>Vaccine response test (tetanus and pneumococcal)</td>
<td>As an aid in the diagnosis of antibody immunodeficiency</td>
</tr>
<tr>
<td>International Patient Organisation for Primary Immunodeficiencies (IPOPI)</td>
<td>Numeration of lymphocyte subtypes, namely CD4 (as in HIV), CD8, CD20, CD16/56 cells</td>
<td>As an aid in the diagnosis of primary and secondary immunodeficiencies</td>
</tr>
<tr>
<td>International Patient Organisation for Primary Immunodeficiencies (IPOPI)</td>
<td>Immunoglobulin plasma levels (IgG, IgA, IgM)</td>
<td>To identify patients with low immunoglobulins and monitor replacement</td>
</tr>
<tr>
<td>International Patient Organisation for Primary Immunodeficiencies (IPOPI)</td>
<td>Plasma and urine protein electrophoresis and immunofixation</td>
<td>As an aid in the diagnosis of primary and secondary immunodeficiencies. As an aid in the diagnosis of monoclonal plasma cell disorders (e.g. multiple myeloma)</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Kato-Katz</td>
<td>Diagnosis of STH and schistosomes</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Guaiac fecal occult blood test (gFOBT).</td>
<td>Screening &amp; diagnosis of colorectal cancer</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Faecal immunochemical test</td>
<td>Screening &amp; diagnosis of colorectal cancer</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Alpha fetoprotein (AFP) immunoassay</td>
<td>For liver and germ cell cancer diagnosis, prognosis and disease monitoring</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Basic panel with Immunohistochemical testing (IHC) for lymphoma</td>
<td>As an aid in the diagnosis, sub-classification, prognosis and treatment of lymphoma, including HIV- associated conditions.</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Papanicolaou (Pap) smear test</td>
<td>Screening for cervical cancer and for triage testing after a positive HPV result to avoid overtreatment of cervical lesions.</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Prostate specific antigen</td>
<td>As an aid in diagnosis, prognosis and surveillance for prostate cancer</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Detection of BCR-ABL1 and ABL1 transcripts (NAT)</td>
<td>Diagnosis and therapeutic monitoring of chronic myelocytic leukemia (CML) and CML variants (neutrophilic-CML) and prognosis of acute lymphoblastic leukemia (ALL).</td>
</tr>
</tbody>
</table>
## Submissions received

<table>
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<tr>
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</thead>
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<tr>
<td>World Health Organization</td>
<td>Lactate dehydrogenase (LDH) activity</td>
<td>As an aid in the prognosis and monitoring of hematological malignancies (lymphoma) and solid tumors</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Immunohistochemical testing (IHC) for the evaluation of the over-expression of the Receptor tyrosine-protein kinase erbB-2 or human epidermal growth factor receptor 2 (HER2)</td>
<td>As an aid in breast cancer diagnosis, prognosis &amp; treatment</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Immunohistochemical testing (IHC) for the detection of estrogen (ER) and progesterone (PGR) receptors</td>
<td>As an aid in breast cancer diagnosis, prognosis &amp; treatment</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Quantitative determination of the sum of human chorionic gonadotropin (hCG) plus the beta-hCG (ECLIA)</td>
<td>As an aid in germ cell tumour diagnosis and surveillance</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Essential panel of antibodies for flow cytometry for leukemia</td>
<td>As an aid in the diagnosis of acute leukemias</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Basic panel with Immunohistochemical testing (IHC) for solid tumors</td>
<td>As an aid in the diagnosis, subclassification, prognosis and treatment of solid tumors with an emphasis on childhood cancer</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>rK39 rapid diagnostic test - Leishmaniasis</td>
<td>For the diagnosis of leishmanial infection due to L. donovani in South-East Asia and East Africa</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Dengue virus antibody (IgM) EIA or RDT</td>
<td>Population survey and as an aid in the diagnosis of Dengue virus</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Dengue virus antigen (NS1) EIA or RDT</td>
<td>Population survey and as an aid in the diagnosis of Dengue virus</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Dengue virus nucleic acid test (NAT)</td>
<td>Population survey and as an aid in the diagnosis of Dengue virus</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Rapid plasma reagin</td>
<td>As an aid in the diagnosis of syphilis</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Zika virus nucleic acid test (NAT)</td>
<td>As an aid in the diagnosis of Zika virus infection</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Zika virus IgM Immunoassay</td>
<td>As an aid in the diagnosis of Zika virus infection</td>
</tr>
<tr>
<td>Global Sepsis Alliance</td>
<td>Procalcitonin (PCT) test (immunoassay)</td>
<td>Early identification of sepsis patients with bacterial infections</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Flu IA RDT</td>
<td>As an aid in the diagnosis of influenza</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Flu PCR</td>
<td>As an aid in the diagnosis of influenza</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Therapeutic drug monitoring (TDM) IVDs</td>
<td>For early initial detection of a cholera outbreak</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Cholera RDT</td>
<td>For early initial detection of a cholera outbreak</td>
</tr>
</tbody>
</table>
3. General laboratory tests

Process for review of additional general pathology laboratory tests

Available WHO guidance, recommendations by SAGE members, research commissioned by WHO

Proposed list of general laboratory tests

Review by SAGE IVD working group on General Lab tests and EDL secretariat

Proposed list published on WHO website

SAGE IVD recommend inclusions & exclusions to WHO

SAGE IVD recommendations presented to WHO DG
3. General laboratory tests

- Tests used in multiple conditions, and to support the prescription of many different medicines.

- For example Complete Blood Count is relevant to:
  - 187 conditions
  - 270 of the 446 medicines in the Essential Medicines List

- The 2018 EDL contains:
  - 12 test categories in primary care
  - 23 test categories for laboratory facilities
    - Grouped into Haematology, Clinical Chemistry, Blood Transfusion and Microbiology
3. Selection of additional general laboratory tests

1. EDL Secretariat reviewed:
   • Higher priority tests in Schroeder et al (2018)
   • WHO list of priority medical devices for cancer management (2017)
   • Proposals from the SAGE-IVD members

2. Tests were then reviewed by the General Laboratory Working Group of SAGE IVD.

3. List then reviewed by SAGE IVD.

3. New general laboratory tests

- Need to broaden scope to support of disease-specific submissions, not only in infectious diseases but also in cancer and immunodeficiency.
- New division – Anatomical Pathology
- New test categories:
  - 5 in Clinical Chemistry
  - 5 in Haematology
- Expansion of test categories already in the 2018 EDL
  - 2 in Clinical Chemistry
  - 2 in Haematology
- Therapeutic Drug Monitoring was considered to belong in a special category, and was reviewed by independent experts.
4. Therapeutic Drug monitoring

Process for inclusion of therapeutic drug monitoring tests

Prioritization:

**High** (most authors consider TDM useful even for noncritically ill patients): amikacin, gentamicin, phenytoin, lithium

**Moderate** (TDM useful in patients with co-treatments or concomitant clinical complications [e.g., impaired renal function]): vancomycin, methotrexate, cyclosporin

**Low** (careful clinical assessment is enough for most cases, or there are evidences that there are no differences between patients with and without TDM): digoxin, phenobarbital, carbamazepine, valproate
Public comments received

A total of 51 external comments were received

7 external organizations

- Médecins Sans Frontières (MSF)
- Roche Molecular Systems, Roche Diagnostic Centralised and POC solutions, Roche Tissue Diagnostic
- International Federation of Clinical Chemistry and Laboratory Medicine
- Global Medical Technology Alliance (GMTA) and the Global Diagnostics Alliance (GDA)
- Clinton Health Access Initiative (CHAI)
- Treatment Action Group (TAG)

6 types of comments

- General comments
- Change in the level of the healthcare system for tests already listed
- Change in test purpose (e.g. addition of intended population)
- Changes in assay formats listed
- Changes in specimen types listed
- Comments of full submissions
Country implementation

*The EDL is only a list until it is adopted by countries to support access to in vitro diagnostics testing*
6. Global Implementation From EDL to access of IVDs

WHO HQ
- Call for new tests to be added general and disease specific
- Review by WHO
- Public consultation
- Recommendations by SAGE IVD
- Publication of a list including test type, test purpose and link to WHO guidance

Country and health facilities
- WHO EDL
- Prioritized national list
- Local needs: epidemiology, resources, committee

Final users
- National reference lab
- 2 and 3er level
- Primary health care PHC (self testing)
Guidance for country implementation

Next steps after EDL.

1. Develop good quality EDL type products
2. Sell/lease the technologies
3. Get regulatory approval for market in regions or countries
4. Provide ongoing support, training, consumables, affordable and good quality

Role of industry

Develop / integrate Technical specifications for procurement or leasing

Procurement / leasing / payment mechanisms / reimbursement

Installation / user training / Operating costs - (consumables and reagents)
WHO plan for supporting country implementation

Develop Guidance Document for EDL Implementation

1. Baseline data on which countries have IVD lists

2. Collect the challenges and successes experienced by countries who have developed and implemented a program of access to IVDs

3. Develop guidance steps to support country implementation: including regulation, procurement, supply and use.

4. SAGE IVD Implementation Working Group review

5. Develop implementation pilot programme in 3 selected countries to be executed over 18 – 24 months

6. Prepare technical specifications to support procurement

7. Finalise guidance document based on country implementation experience.

WHO welcomes your collaboration
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