# Webinar: Open session day
# 4th Meeting of the Strategic Advisory Group of Experts on IVDs

World Health Organization

14 November 2022

Geneva, Switzerland

# Open session day
# 4th Meeting of the Strategic Advisory Group of Experts on IVDs

## Housekeeping rules

- Please share your questions and comments through the Q&A feature
- Questions and comments will be addressed online as well as orally (as time permits) during the webinar Q&A session
- Questions not answered during the time of the open session will be addressed afterward and posted on the WHO website
- This webinar will be recorded

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# Agenda

| Time | Session | Speaker |
|---|---|---|
| 14h02 | Opening remarks | **Dr Mariângela Simão**<br>Assistant Director-General,<br>Access to Medicines and Health Products division, WHO HQ |
| 14h07 | 4th SAGE IVD meeting Objectives | **Dr Francis Moussy**<br>Lead, Secretariat of the WHO Model List of Essential In Vitro Diagnostics, WHO HQ |
| 14h12 | EDL: overview, scope and methodology for its review and update | **Dr Ana Aceves Capri**<br>Technical Officer, WHO EDL Secretariat, WHO HQ |
| 14h38 | The EDL and its relationship with other WHO model/priority lists:<br>• Essential medicines list (EML)<br>• Priority assistive products list (APL)<br>• Priority Medical Devices list (MEDEVIS) | **Dr Benedikt Huttner**<br>Team Lead, Essential Medicines List (EML), WHO HQ<br>**Dr Wei Zhang**<br>Technical Officer, Access to Assistive Technology, WHO HQ<br>**Ms Adriana Velázquez Berumen**<br>Team Lead, Medical Devices and In Vitro Diagnostics, WHO HQ |
| 15h11 | The EDL at country level: National EDLs and related IVD activities at regional level | **Mr Stephen Himley**<br>Technical Officer (Health Technologies), WHO Regional Office for South-East Asia (SEARO)<br>**Mr Alexandre Lemgruber**<br>Regional Advisor, Health Technologies, PAHO |
| 15h32 | Q&A session | |
| 16h00 | End of day | |

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# Meeting objectives

The objective of the 4th SAGE IVD meeting is to discuss and make recommendations on policies and strategies related to in vitro diagnostics and the EDL, including:

- Review the applications received for the EDL 4
- Make recommendations for the fourth WHO model list of essential in vitro diagnostics (EDL)
- Discuss current strategies and make recommendations on the way forward to increase availability, access, and proper use of in vitro diagnostics
- Collect input from stakeholders during the open session

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# WHO model list of essential in vitro diagnostics (the EDL)

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# Essential in vitro diagnostics

- Essential in vitro diagnostics are those that satisfy the priority health care needs of the population and are selected with due regard to disease prevalence, public health relevance, evidence of efficacy and accuracy and comparative cost-effectiveness.

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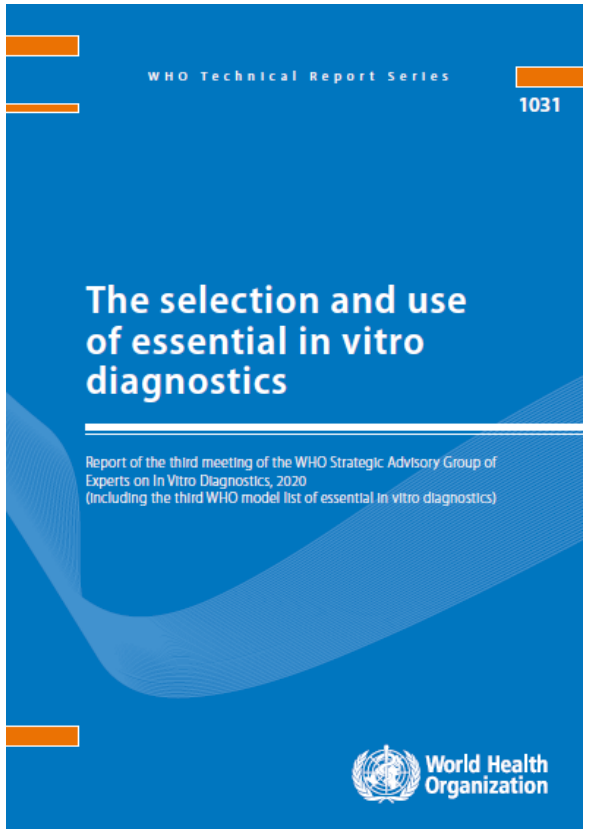
# What is the EDL?




The WHO model list of essential in vitro diagnostics (EDL) is a policy document, based on scientific evidence, consisting in a register of categories of IVD tests and recommendations for those test (assay format, test purpose, specimen type, healthcare setting).

- First edition (May 2018)
- Second edition (November 2019)
- Third edition (January 2021)

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# Example of EDL 3 listing

| I.b Disease-specific IVDs for use in community settings and health facilities without laboratories *(continued)* | | | | | | |
|---|---|---|---|---|---|---|
| Disease | Diagnostic test | Test purpose | Assay format | Specimen type | WHO prequalified or recommended products | WHO supporting documents |
| Diabetes mellitus *continued* | Haemoglobin A1c (HbA1c) | To diagnose and monitor diabetes mellitus | Handheld and small analysers | Capillary whole blood | N/A | HEARTS-D: diagnosis and management of type 2 diabetes (2020) https://www.who.int/publications/i/item/who-ucn-ncd-20.1 https://www.who.int/health-topics/diabetes#tab=tab_1 |
| Hepatitis B virus (HBV) infection | Hepatitis B surface antigen (HBsAg) | To screen for HBV infection, or to aid in the diagnosis of chronic and acute HBV infection: infants > 12 months of age, children, adolescents and adults | RDT | Capillary whole blood Venous whole blood[10] | Public reports of WHO prequalified IVDs https://extranet.who.int/pqweb/vitro-diagnostics/prequalification-reports/whopr?field_whoprcategory=63 | Guidelines on hepatitis B and C testing (February 2017) https://apps.who.int/iris/handle/10665/254621 https://www.who.int/news-room/fact-sheets/detail/hepatitis-b |

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# Objectives of the EDL

- **The EDL is intended to support IVD policy development to improve people access to IVD testing and clinical laboratory services through:**
- Provision of evidence-based guidance for countries to create or update their national EDL
- Prioritization of IVD tests that should be available at different levels of the healthcare system
- Provision of information to United Nations agencies and NGOs that support the selection, procurement, supply or donation of IVDs
- Provision of guidance to the private health technology and manufacturing sectors about the IVD priorities required to address global health issues

**The goal of the EDL is to help countries advance UHC, address health emergencies and promote healthier populations, which are the three strategic priorities of the WHO Thirteenth General Programme of Work (2019 – 2023)**

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# Scope of EDL 3

The EDL includes general and disease-specific IVDs for non-communicable disease (NCD) and infectious diseases

| General tests | Disease-specific |
|---|---|
| Anatomical pathology | Aspergillosis |
| Blood typing | Cancer |
| Clinical chemistry | Chagas disease |
| Clinical microbiology | Cholera |
| Clinical pathology | COVID-19 |
| Haematology | Diabetes mellitus |
| Pregnancy testing | Endocrine disorders |
| | Hepatitis B |
| | Hepatitis C |
| | HIV |
| | Human papillomavirus |
| | Influenza |
| | Malaria |
| | Neglected tropical diseases |
| | Pneumocystis pneumonia |
| | Primary immunodeficiencies |
| | Streptococcal pharyngitis |
| | Sickling disorders |
| | Sexually transmitted infections |
| | Syphilis |
| | Tuberculosis |
| | Vaccine preventable diseases |
| | Visceral leishmaniasis |
| | Zika virus |

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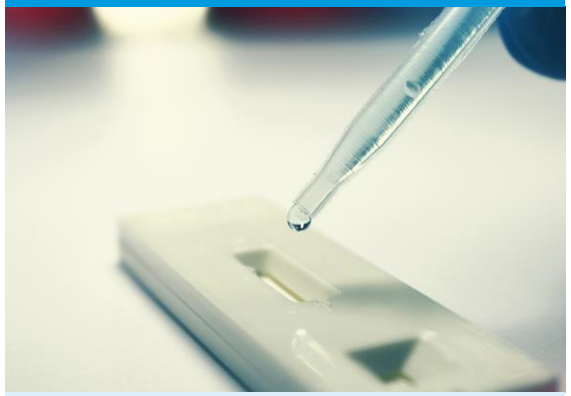
# Presentation of the EDL 3

The WHO EDL is presented by health-care facility level in **two tiers** and a Do Not Do recommendations section

**Community settings and health facilities without laboratories**



**I.a** General tests (arranged by discipline)
**I.b** Disease-specific tests (arranged by disease)

**Health care facilities with clinical laboratories**

**II.a** General tests (arranged by discipline)
**II.b** Disease-specific tests (arranged by disease)
**II.c** Bloods screening tests

**Do Not Do recommendations**

Refer to test categories that have been listed for discontinuation

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# Example of EDL 3 listing

| I.b Disease-specific IVDs for use in community settings and health facilities without laboratories *(continued)* | | | | | | |
|---|---|---|---|---|---|---|
| Disease | Diagnostic test | Test purpose | Assay format | Specimen type | WHO prequalified or recommended products | WHO supporting documents |
| Diabetes mellitus *continued* | Haemoglobin A1c (HbA1c) | To diagnose and monitor diabetes mellitus | Handheld and small analysers | Capillary whole blood | N/A | HEARTS-D: diagnosis and management of type 2 diabetes (2020) https://www.who.int/publications/i/item/who-ucn-ncd-20.1 https://www.who.int/health-topics/diabetes#tab=tab_1 |
| Hepatitis B virus (HBV) infection | Hepatitis B surface antigen (HBsAg) | To screen for HBV infection, or to aid in the diagnosis of chronic and acute HBV infection: infants > 12 months of age, children, adolescents and adults | RDT | Capillary whole blood Venous whole blood[10] | Public reports of WHO prequalified IVDs https://extranet.who.int/pqweb/vitro-diagnostics/prequalification-reports/whopr?field_whoprcategory=63 | Guidelines on hepatitis B and C testing (February 2017) https://apps.who.int/iris/handle/10665/254621 https://www.who.int/news-room/fact-sheets/detail/hepatitis-b |

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# Review and updating of the EDL

- The EDL is updated regularly, with periodic calls for submission of applications
- Applications can be submitted by:
  - Stakeholders, such as Member States, academia, professional organizations, NGOs or companies in the IVD industry
  - WHO regional or country offices
  - WHO HQ departments
- The EDL secretariat oversees submissions, and the **SAGE IVD** is responsible for reviewing applications and making recommendations

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# Strategic Advisory Group of Experts on in vitro diagnostics

- The **SAGE IVD** was conceived in 2018 as an advisory body on matters of global policy and strategy related to IVDs, including advising WHO on the tests to be included in the EDL

    - SAGE IVD members serve in their personal capacities and represent the broad range of disciplines required to advise on the many aspects of IVDs and other clinical laboratory related activities
    - Geographical representation: experts from all the WHO regions
    - Gender balance
    - Conflict of interest is managed according to rules and procedures from the WHO Office of Compliance, Risk Management and Ethics

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# 2021 SAGE IVD panel

Dr Amina Hançali, Morocco.

Prof Anurag Bhargava, India

Dr Cassandra Kelly-Cirino, Switzerland

Dr Dario Trapani, Italy

Dr Sadia Shakoor, Pakistan

Dr Jean-Pierre Chanoine, Canada

Prof Rashad Abdul-Ghani, Yemen

Dr Lee Schroeder, United States of America

Dr Patricia J. García, Peru

Mr. Paulinus Offutalu, Nigeria

Dr Kenneth Fleming, United Kingdom

Dr Ravnit Gravel, South Africa

Dr Francis Ndowa, Zimbabwe

Prof William Sewell, Australia

Dr Lyu Yunfeng, China

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https://www.who.int/groups/who-strategic-advisory-group-of-experts-on-in-vitro-diagnostics

# Criteria for listing test categories in the EDL

- **Public health impact** of the disease and the test category, as determined by disease burden and other published evidence
- Availability of published **evidence on clinical utility**
- Availability of published **evidence of diagnostic and clinical accuracy**
- **Availability of commercial IVD products**, as confirmed by adequate data on quality, safety, performance and regulatory status
- Operational characteristics and infrastructure required, such as intended user(s), training requirements, specimen type, storage conditions, energy requirements and associated equipment
- Availability of evidence on cost–effectiveness
- Equity and human rights issues
- Ethical considerations

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# The update of the EDL is a rigorous evidence-based process

| | |
|---|---|
| **Step 1** | Pre-submission for addition of a new test category assessed for completeness by the EDL secretariat and circulated to relevant WHO departments. A full submission is invited if appropriate. |
| **Step 2** | EDL secretariat reviews for completeness all **type of submissions**: full submissions for **addition of a new test category**, and submissions for **edits**, **delisting**, **additional evidence** for IVDs conditionally listed **and Do Not Do recommendations**. |
| **Step 3** | Each submission is peer-reviewed by at least two members of the SAGE IVD, who formulate draft recommendations for consideration by the full SAGE IVD during meeting(s) for selection. |
| **Step 4** | The evidence provided in each submission is reviewed and assessed for its strength and quality by a methodologist. |
| **Step 5** | All applications and expert reviews are published on the WHO website for full transparency and public comment before the selection meeting(s). |
| **Step 6** | **SAGE IVD meeting**: SAGE IVD members and methodologists present their recommendations for each application to the full SAGE IVD for discussion. |
| **Step 7** | The SAGE IVD reaches a decision for each submission by consensus, documents the reasons for its decision and makes a recommendation to the WHO Director-General. |
| **Step 8** | The Director-General approves the list. |

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# Planning for the EDL 4

## What tests are missing?  Identifying high priority IVDs for EDL 4

From the review of WHO publications, past SAGE IVD recommendations and published work on IVDs for the medicines listed in the WHO EML, we identified 71 candidate tests to inform EDL 4 call for submissions, additional discussions took place and the SAGE IVD reach consensus on the following 23 tests categories:

1. therapeutic drug monitoring Amikacin
2. therapeutic drug monitoring Gentamicin
3. therapeutic drug monitoring Phenytoin
4. therapeutic drug monitoring Lithium
5. therapeutic drug monitoring Methotrexate
6. **nucleic acid testing, *N. meningitidis***
7. antigen, Entamoeba
8. Testosterone, total
9. Protein electrophoresis (in serum and urine)
10. Immunofixation electrophoresis
11. Free light-chain test (in serum)
12. Antibodies against Scrub Typhus (IgM)
13. Antibodies against Leptospira (IgM)
14. serology, Yellow fever
15. nucleic acid testing, Diphtheria
16. IVDs for *Bordetella pertussis*
17. IVDs for Poliovirus
18. IVDs for Rotavirus
19. Lead
20. Hepatitis Delta (RDTs, EIA and RNA PCR)
21. **Hepatitis E (RDTs, EIA and RNA PCR)**
22. **17 hydroxyprogesterone**
23. **Parathyroid hormone**

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# EDL 4 submissions

## Addition of new IVD categories:

1. High-sensitivity Troponin I test (hs-cTnI)
2. RDT to anti-Hepatitis E Virus IgM
3. Hepatitis E Virus NAT
4. ELISA to anti-Hepatitis E Virus IgM
5. 17-Hydroxy Progesterone
6. Kleihauer-Betke acid-elution test
7. Parathyroid hormone
8. Meningitis/Encephalitis PCR Panel
9. ABO and Rh factor POC dry format card

## Editions:

10. Glucose
11. M. tuberculosis DNA

## Do Not Do Recommendations

12. Typhoid serological tests

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# Planning for the EDL 4

## January - July 2022

Open call for submissions:

Addition of new IVD categories

Editions

Delisting

Do Not Do recommendations

Additional evidence in support of previous submissions (conditional listing)

## September - October 2022

Review of the submissions and Public consultation

## November 2022

Review of comments from public consultation

**SAGE IVD meeting: November 14-18**

## January - March 2023

Development of the report of the SAGE IVD meeting, including the EDL 4

## April 2023

EDL4 launch and publication

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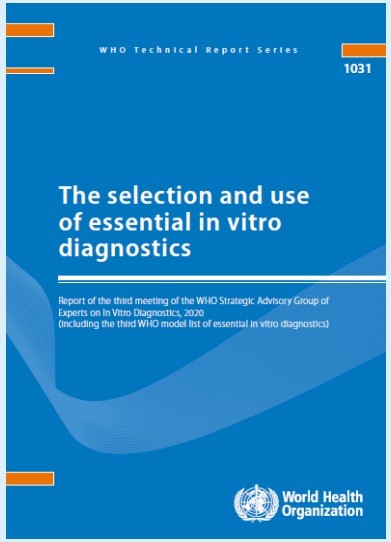
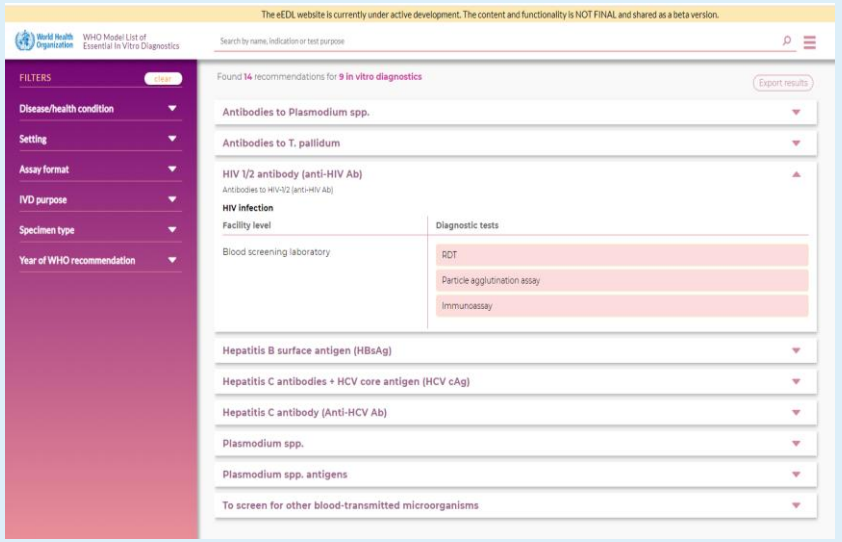
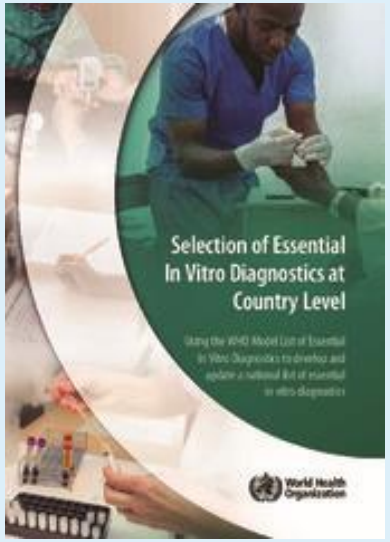
# Tools to support countries

1. WHO Technical Report Series: The selection and use of essential IVDs
2. Electronic EDL (eEDL)
3. Selection of essential in vitro diagnostics at country level: using the WHO Model List of Essential In Vitro Diagnostics to develop and update a national list of essential in vitro diagnostics
4. Technical specifications to support selection and procurement of IVD products (work under development)

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# Additional Information

- **EDL Secretariat contact:** EDLsecretariat@who.int
- **Electronic eEDL (beta version):** https://edl.who-healthtechnologies.org/
- **WHO web page on the EDL:** https://www.who.int/teams/health-product-policy-and-standards/assistive-and-medical-technology/medical-devices/selection-access-and-use-in-vitro
- **WHO IVD web page:** https://www.who.int/health-topics/in-vitro-diagnostics#tab=tab_1
- **WHO Medical Devices web page:** https://www.who.int/health-topics/medical-devices#tab=tab_1

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# Thank you

For more information, please contact:
Name:  Dr Ana Elisa Aceves Capri
Title: Technical Officer
Email: acevesa@who.int

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# The EDL and its relationship with other WHO model/priority lists

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# The EDL and its relationship with the Essential Medicines List (EML)

Open session, November 14, 2022

4th Meeting of the Strategic Advisory Group of Experts on IVDs

Benedikt HUTTNER

Secretray Expert Committee on the Selection and Use of Essential Medicines

bhuttner@who.int

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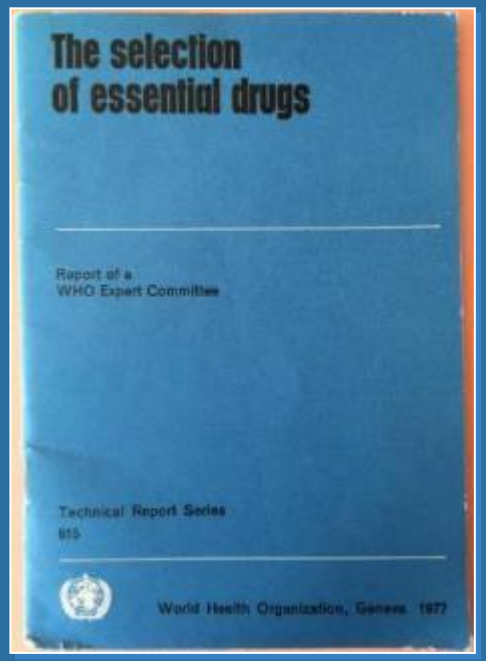
# *“Treatment without diagnosis is a form of quackery”*

P

Paris. Can Psychiatr Assoc J. 1975 Jun;20(4):305-7.

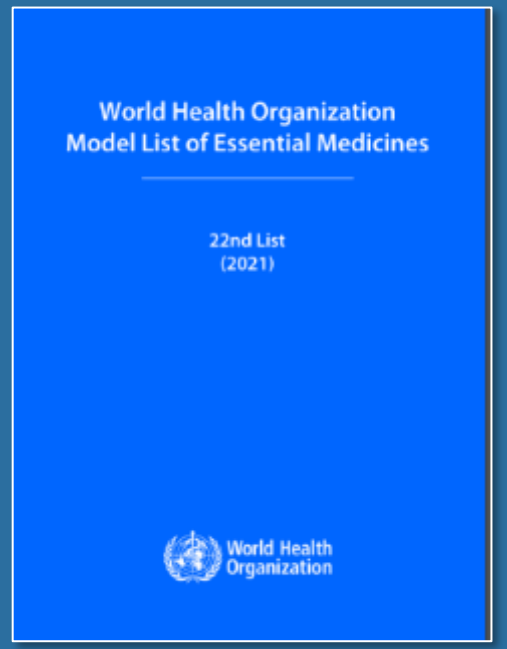
# The WHO Model Lists of Essential Medicines (EML) 1977 - 2021




**1977** **240 medicines**

**New additions / changes 2021 (88 applications)**

- Long-acting insulin analogues
- Medicines for smoking cessation
- Cancer medicines (enzalutamide, everolimus, ibrutinib, rasburicase; new indications for children,…)
- Sumatriptan for acute migraine
- Dental preparations (fluoride toothpaste,…)
- Reserve antibiotic (cefiderocol)
- Antifungal (echinocandins)
- …




**EML: 479 medicines**
**EMLc: 350 medicines**

2007 first EMLc

**2021**

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## 23rd meeting of the WHO Expert Committee on Selection and Use of Essential Medicines

Virtual meeting 21June to 2 July 2021

88 applications reviewed

- **The EC recommended:**
  - Addition of 20 new medicines to the EML
  - Addition of 17 new medicines to the EMLc
  - Additional indications for 28 already listed medicines
  - Additional formulations of 23 already listed medicines
  - Deletion of 2 medicines and of specific formulations of 13 medicines
  - Update of 72 square box listings, removal of 7 square box listings, review of 23 square box listings recommended

- **The EC did <u>not</u> recommend:**
  - 25 proposals for inclusion, change or deletion for 28 medicines, medicine classes or formulations

# Request for Advice from the Expert Committee on Selection and Use of Essential Medicines on Prioritization of Medicines Requiring **Therapeutic Drug Monitoring**

| PRIORITY | MEDICINE |
|---|---|
| **High**<br>(most authors consider TDM useful even for non-critically ill patients) | • Amikacin<br>• Gentamicin<br>• Lithium<br>• Phenytoin |
| **Moderate**<br>(TDM considered useful in patients with co-treatments or concomitant clinical complications [e.g. impaired renal function]) | • Cyclosporin<br>• Methotrexate<br>• Vancomycin |
| **Low**<br>(careful clinical assessment is enough for most cases, or there is evidence that there are no differences between patients with and without TDM) | • Carbamazepine<br>• Digoxin<br>• Phenobarbital<br>• Sodium valproate |

The Expert Committee advised that it considered the proposed prioritized list of medicines to be appropriate with the exception of methotrexate

https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/23rd-expert-committee/o3-report

# Therapeutic drug monitoring advice for SAGE-IVD

## METHOTREXATE

- Use of methotrexate is common in clinical practice for several diseases
- EC recommended to consider TDM of methotrexate as a **high priority** to reduce the incidence of toxicity, especially when methotrexate is used in high-dose treatment protocols

## EVEROLIMUS AND TACROLIMUS

- Everolimus (subependymal giant cell astrocytoma) and tacrolimus (prevention and treatment of rejection in organ transplantation) added to 2021 EML
- EC advised that these medicines be considered as **moderate priority** candidates for TDM assays

## VORICONAZOLE

- On EML since 2017 for treatment of chronic pulmonary aspergillosis and acute invasive aspergillosis
- EC advised that voriconazole be considered a **moderate priority** candidate for TDM assays
- Pharmacokinetic characteristics and potential for drug–drug interactions

The Selection and Use of Essential Medicines (2021) - TRS 1035

For the addition of new IVD categories for EDL4 we are specially inviting applications for the following IVD categories:

1. therapeutic drug monitoring Amikacin
2. therapeutic drug monitoring Gentamicin
3. therapeutic drug monitoring Phenytoin
4. therapeutic drug monitoring Lithium
5. therapeutic drug monitoring Methotrexate
6. nucleic acid testing, N. meningitidis
7. antigen, Entamoeba
8. Testosterone, total
9. Protein electrophoresis (in serum and urine)
10. Immunofixation electrophoresis
11. Free light-chain test (in serum)
12. Antibodies against Scrub Typhus (IgM)
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17. IVDs for Poliovirus
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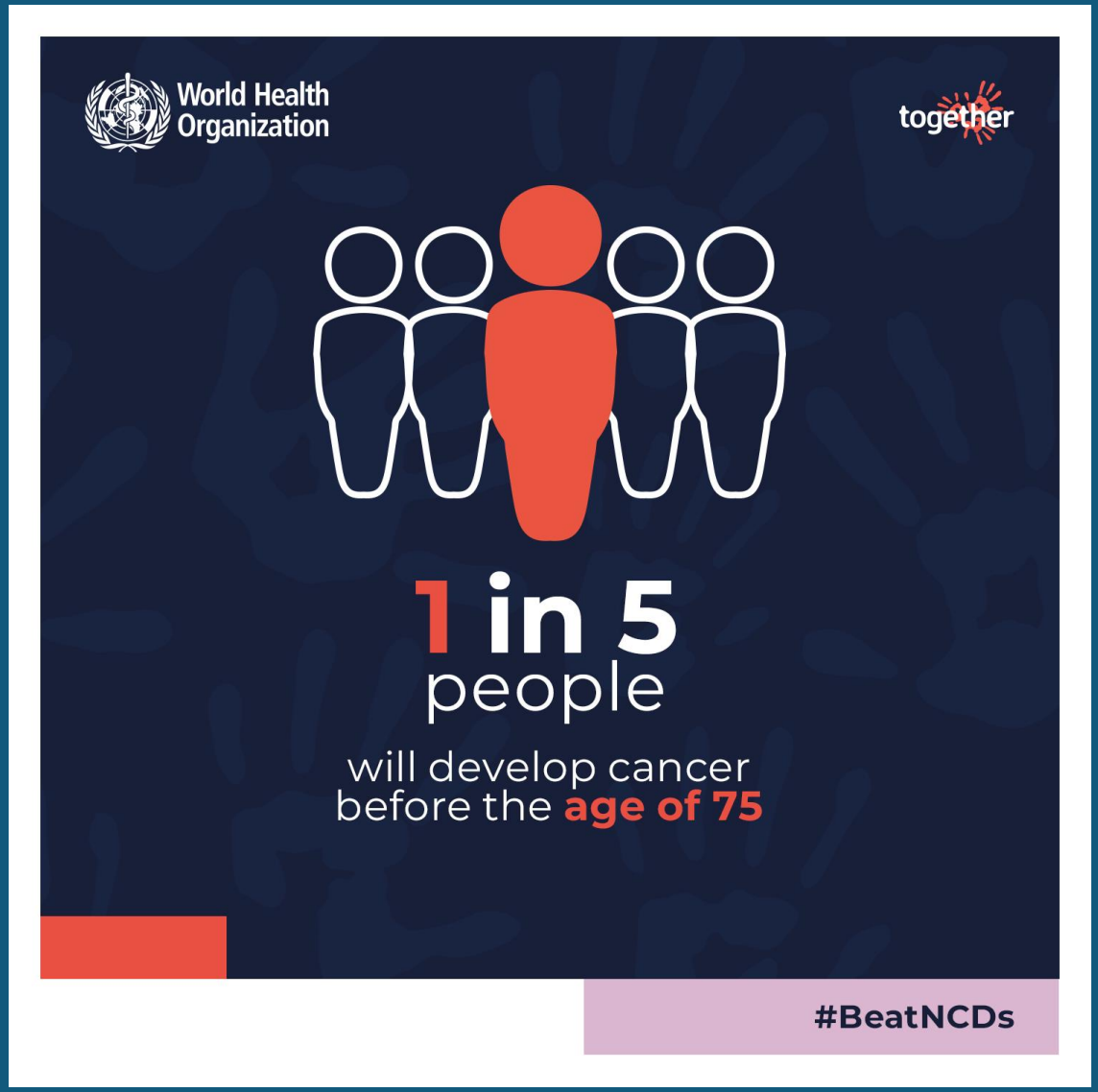
19. Lead
20. Hepatitis Delta (RDTs, EIA and RNA PCR)
21. Hepatitis E (RDTs, EIA and RNA PCR)
22. 17 hydroxyprogesterone
23. Parathyroid hormone

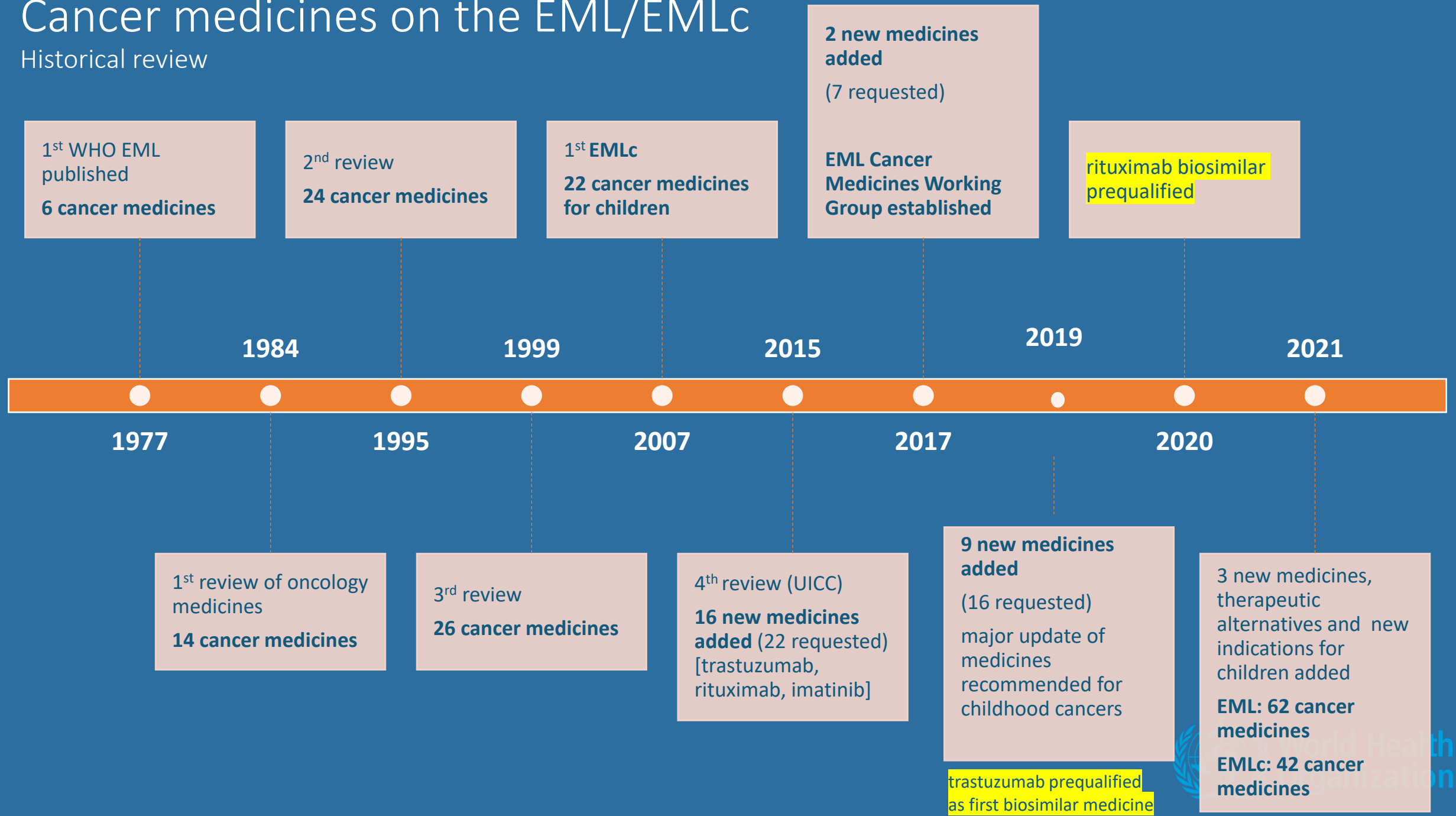
The EDL Secretariat will also consider submissions for IVD categories not mentioned in the above list.

# Cancer medicines

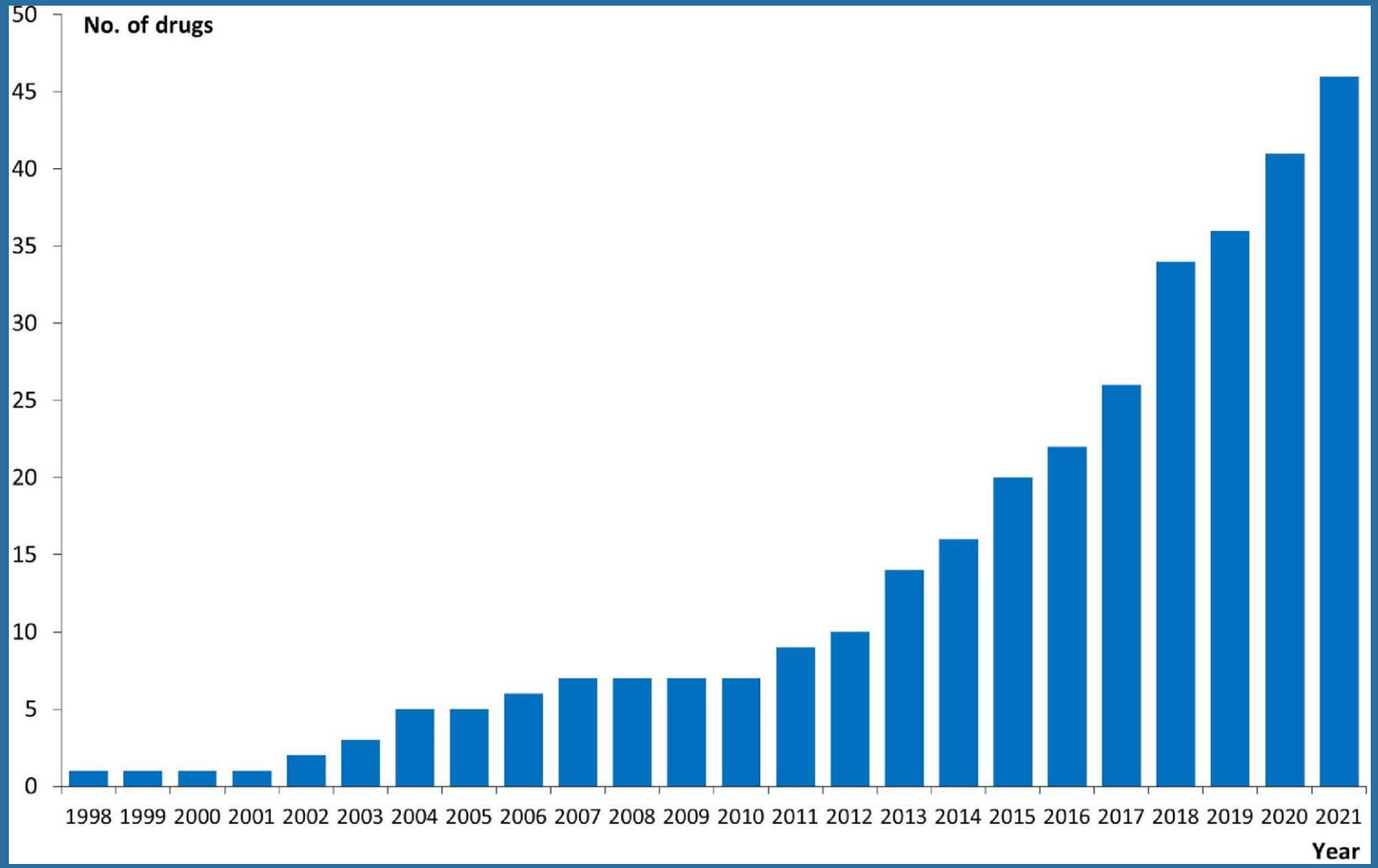


# Cancer medicines on the EML/EMLc

## Historical review



Cumulative number of FDA approved oncological and hematological medicine companion diagnostic combinations by year.




Jørgensen JT.Cancer Treat Res Commun. 2021;29:100492.

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# Antibiotics

# Reserve antibiotics

Reserve group of antibiotics includes antibiotics that still have significant levels of activity against some of the multidrug-resistant bacteria listed in the WHO priority pathogen list, including bacteria which are resistant to most or all of the EML antibiotics in the Access and Watch groups

**Table 41.1 – Expected activity of Reserve antibiotics against third-generation cephalosporin- and carbapenem-resistant bacteria based on the type of beta-lactamase produced**

| Type of beta-lactamase | ESBL[a] | KPC[b] | NDM, VIM, IMP[b] | AmpC | OXA-48[b] | Non-fermenters[c] |
|---|---|---|---|---|---|---|
| **Ambler class[d]** | A[e] | A[e] | B (MBLs) | C[e] | D[e] | NA |
| Cefiderocol | + | + | + | + | + | +[f] |
| Ceftazidime+ avibactam | + | + | – | + | + | – *Acinetobacter baumannii* |
| | | | | | | + *Pseudomonas aeruginosa* |
| Fosfomycin (IV) (consider using only in combination therapy) | + | +/– | +/– | + | +/– | – *Acinetobacter baumannii* |
| | | | | | | +/– *Pseudomonas aeruginosa* |
| Meropenem+ vaborbactam | + | + | – | + | – | +/– |
| Plazomicin | + | + | +/– | + | + | – |
| Polymyxin B and colistin | + | + | + | + | + | + |

ADULTS

# Community-acquired pneumonia



## Definition

An acute illness affecting the lungs usually presenting with cough, sputum production, and rapid and difficult breathing with a new or worsening pulmonary infiltrate on a chest radiograph

## Most Likely Pathogens

**"Typical" Bacteria:**

- ***Streptococcus pneumoniae*** (most cases)
- *Haemophilus influenzae* (chronic lung diseases, smoking)
- *Moraxella catarrhalis* (chronic lung diseases, smoking)
- *Staphylococcus aureus* (often associated with influenza)
- *Enterobacterales* (severe comorbidities, e.g. chronic lung diseases, dementia, stroke)

**"Atypical" Bacteria:**

- *Mycoplasma pneumoniae* (more frequent in young adults)
- *Chlamydia pneumoniae* and *psittaci* (more frequent in young adults)
- *Legionella* spp. (chronic lung diseases or other underlying illness, travel, exposure to hot tubs)
- *Coxiella burnetii* (rural areas, exposure to livestock)

**Respiratory Viruses:**

- Influenza viruses (A and B)
- Respiratory syncytial virus (RSV)
- Metapneumovirus
- Parainfluenza virus
- Coronavirus (including SARS-CoV-2)
- Adenovirus
- Rhinovirus
- Other respiratory viruses

**Bacteria to consider in Specific Settings:**

- *Burkholderia pseudomallei* (SE Asia, Australia)
- *Mycobacterium tuberculosis*
- *Pneumocystis jirovecii* (people with HIV or other immunosuppression)

## Investigating for Tuberculosis (TB)

- Consider specific investigations for TB in endemic settings especially in high-risk patients (e.g. HIV)
- A rapid molecular test performed on a single sputum specimen is the preferred first line diagnostic test for pulmonary TB and to detect rifampicin resistance

## Diagnosis

### Clinical Presentation

- New onset (<2 weeks) or worsening cough with fever (≥38.0°C), sputum production, dyspnea, tachypnea, reduced oxygen saturation, crepitations on lung auscultation, chest pain/discomfort without alternative explanation
- Extrapulmonary features (i.e. confusion, disorientation) may predominate in elderly, and immunosuppressed patients and fever may be absent

### Microbiology Tests

**Mild cases:** usually not needed

**Severe cases (to guide antimicrobial treatment):** blood cultures, urinary antigens for *L. pneumophila* and *S. pneumoniae*

**Selected cases (depending on epidemiology and risk factors):** sputum rapid molecular test for *M. tuberculosis* (and the lipoarabinomannan rapid urinary antigen test in severely immunocompromised HIV patients with signs and symptoms of tuberculosis), nasopharyngeal swab for influenza viruses and SARS-CoV-2, HIV testing in settings with high HIV prevalence and in case of recurrent and/or severe pneumonia

### Other Laboratory Tests

**Determine disease severity:** blood urea nitrogen (see CURB-65 Scoring System box), blood pH and gases, white blood cell count

**Differentiate bacterial and viral (taking into account pre-test probability):** C-reactive protein and/or procalcitonin

*Note: tests depend on availability and clinical severity (e.g. blood gases will only be done in severe cases)*

### Imaging

- Chest X-ray not necessary in mild cases
- Infiltrate may not always be evident (e.g. dehydration) and non-infectious etiologies may mimic infiltrates (e.g. lung edema, pulmonary embolism)
- Radiologic appearance cannot be used to accurately predict pathogen

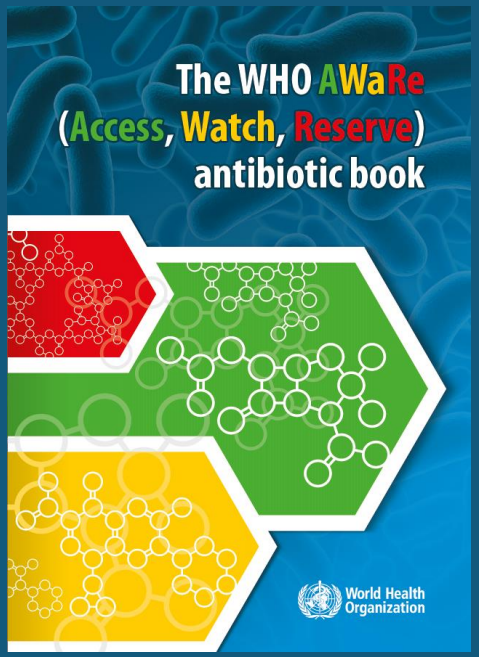



**Table 14.5 – Microbiology tests to consider in certain cases of diarrhoeal disease as indicated in the WHO EDL *(6)***

| Diagnostic test | Purpose of the test | Setting where the test should be available |
|---|---|---|
| Stool culture and antimicrobial susceptibility testing | To detect and identify bacterial species for selection of appropriate antibiotic regimens | Health care facilities with clinical laboratories |
| Stool microscopy | To detect and identify parasites and their ova (eggs) or cysts | Health care facilities with clinical laboratories |
| *Vibrio cholerae* antigen[a] (RDT) | To detect or exclude a cholera outbreak (not for use in case management) | Community settings and health facilities without laboratories |

EDL: Model List of Essential In Vitro Diagnostics; RDT: rapid diagnostic test.
[a] Possible specimens include stool and rectal swab.

Health
ization

# 24th Expert Committee on Selection and Use of Essential Medicines

24 – 28 April 2023 | 20 Avenue Appia - CH-1211 Geneva 27, Geneva, Switzerland

The meeting of the 24th WHO Expert Committee on the Selection and Use of Essential Medici
from 24 to 28 April 2023 at WHO Headquarters in Geneva. The purpose of the meeting will

# Thank you for your attention !

- Special thanks to the EML team (Bernadette Cappello, Lorenzo Moja, Irina Nozdrina),

Cconsultants, WHO colleagues from other departments, experts,….

# More information

Executive Summary, 23rd Expert Committee Meeting

https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.01

22nd WHO Model List of Essential Medicines (2021)

https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.02

8th WHO Model List of Essential Medicines for Children (2021)

https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.03

2021 AWaRe Classification database

https://www.who.int/publications/i/item/2021-aware-classification

WHO Technical Report Series, No. 1035

https://www.who.int/publications/i/item/9789240041134

Information for applicants preparing a submission for the 2023 update

https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2022.01

World Health Organization

# WHO
# Priority Assistive Products List and supporting materials development

an overview

2022.10

# Topics

- Background
- Objectives
- Development plan
- Working groups

# Background

- According to the latest evidence published in Global Report on Assistive Technology, 2.5 billion people need at least one assistive product, and the need is estimated to grow over 3.5 billion people by 2050.

- The 1st WHO Priority Assistive Products List was published in 2016, which contains 50 products across functional domains of cognition, communication, hearing, mobility, seeing and self-care.

- With the technology advancement, new knowledge and evidence, the list needs to be updated based on the latest evidence and practices. And plan for regular updates (e.g. every 2-3 years).

# Objectives

WHO Priority Assistive Products List aims to

- provide a model list to Member States for adoption, adaptation or development of national priority assistive products list.
- provide evidence-informed guidance on selection of assistive products.
- support market shaping and planning for assistive products provision (i.e. financing, production,  procurement, workforce training, service delivery, etc).
- support raising awareness of the need for and the benefits of using assistive products.

# Development plan

- Systematic and transparent methodology development based on experience of other WHO essential health product lists and following recommended process from WHO QNS and GRC.

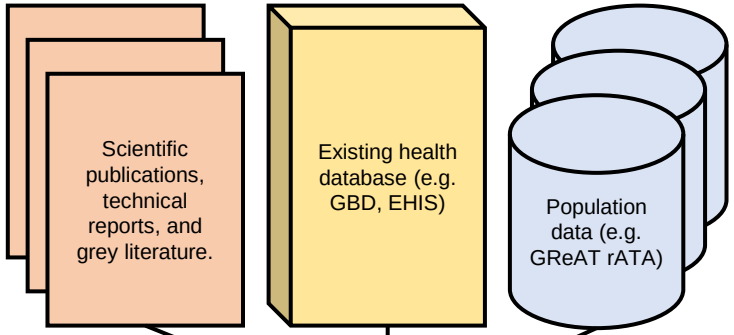
- Development of a prioritization framework using weighted indicators

  The indicators may be related to different aspects of benefits, safety, needs or costs (which may differ for various types of assistive products and functional domains).

- Supporting materials will be developed, e.g., guidance on using the APL, product specifications.

- An online platform of the APL will be developed (eAPL) and integrate supporting materials for efficient technical support and capacity building.

# Development milestones and timeline (as of Oct-22)




**Project scoping and Advisory Group establishment** → **Prioritization methodology development** → **Evidence synthesis and draft list development** → **Consultations and feedback integration** → **Final APL** → **eAPL development**

| – Dec 2021 | Jan – Dec 2022 | Dec 2022 – Feb 2023 | Mar – Apr 2023 | May – Jun 2023 | Jul 2023 |
|---|---|---|---|---|---|
| • Steering group (SG) established<br>• Technical advisory group (TAG) recruited<br>• Onboarding of methodologist | • Planning clearance obtained<br>• APL development methodology approved<br>• Research Groups recruited | • Review and evaluation of evidence report finalized<br>• Draft APL for consultation | • Consultation with stakeholders completed<br>• Draft APL for executive clearance | • Final list cleared for publication and eAPL integration<br>• Development of eAPL started<br>• (Development of supporting material, e.g., how to use the APL) | • Launch of eAPL<br>• (Development of supporting material will start, e.g., product specifications, training, etc.) |

# Working groups


Technical Advisory Group on Assistive Technology

| Working groups | Names |
|---|---|
| Technical Advisory Group | 14-member global expert group as of Oct - 22 |
| Steering Group | Matteo Cesari (WHO Aging);<br>Shelly Chadha (WHO Sensory function, disability & rehab);<br>Yasmin Garcia (PAHO, AT & medical devices);<br>Hyobum Jang (WHO Long-term care);<br>Nathalie Maggay (WPRO AT, rehab, aging and disability);<br>Ameel Mohammad (SEARO AT & rehab);<br>Andrea Pupulin (EURO AT & rehab);<br>Diana Taguembou (AFRO AT, MD, pharm);<br>Mohamad Wehbi (EMRO AT & MD);<br>Diana Zandi (WHO Digital health) |
| Lead editor | Johan Borg |
| Methodologists | Lotty Hooft; Kevin Jenniskens; Bada Yang; Pauline Heus; Michiel Oerbekke; Kim van der Braak; René Spijker<br><br>Cochrane Netherlands, Julius Center for Health Sciences and Primary Care, Utrecht University, University Medical Center Utrecht, The Netherlands |
| Research Group | External research groups and WHO technical units/staff |
| Responsible Technical Officer | Wei Zhang (WHO ATA) |
| Administrative support | Krizzia Melo-Maramba (WHO ATA) |

**SAGE IVD 2022**

**The EDL and its relationship with other WHO model/priority lists: Essential medicines list (EML), Priority assistive products list (APL), Priority Medical Devices list (MEDEVIS)**

14 November 2022

# Priority medical devices and Essential in vitro diagnostics

Adriana Velazquez Berumen,

Team lead medical devices, WHO

World Health Organization

# Agenda

- IVD are medical devices
- Value chain to increase access for all medical devices
- WHO Priority medical devices List
- WHO electronic platforms
- WHA mandates
- Use of WHO Lists
- Challenges
- Way forward

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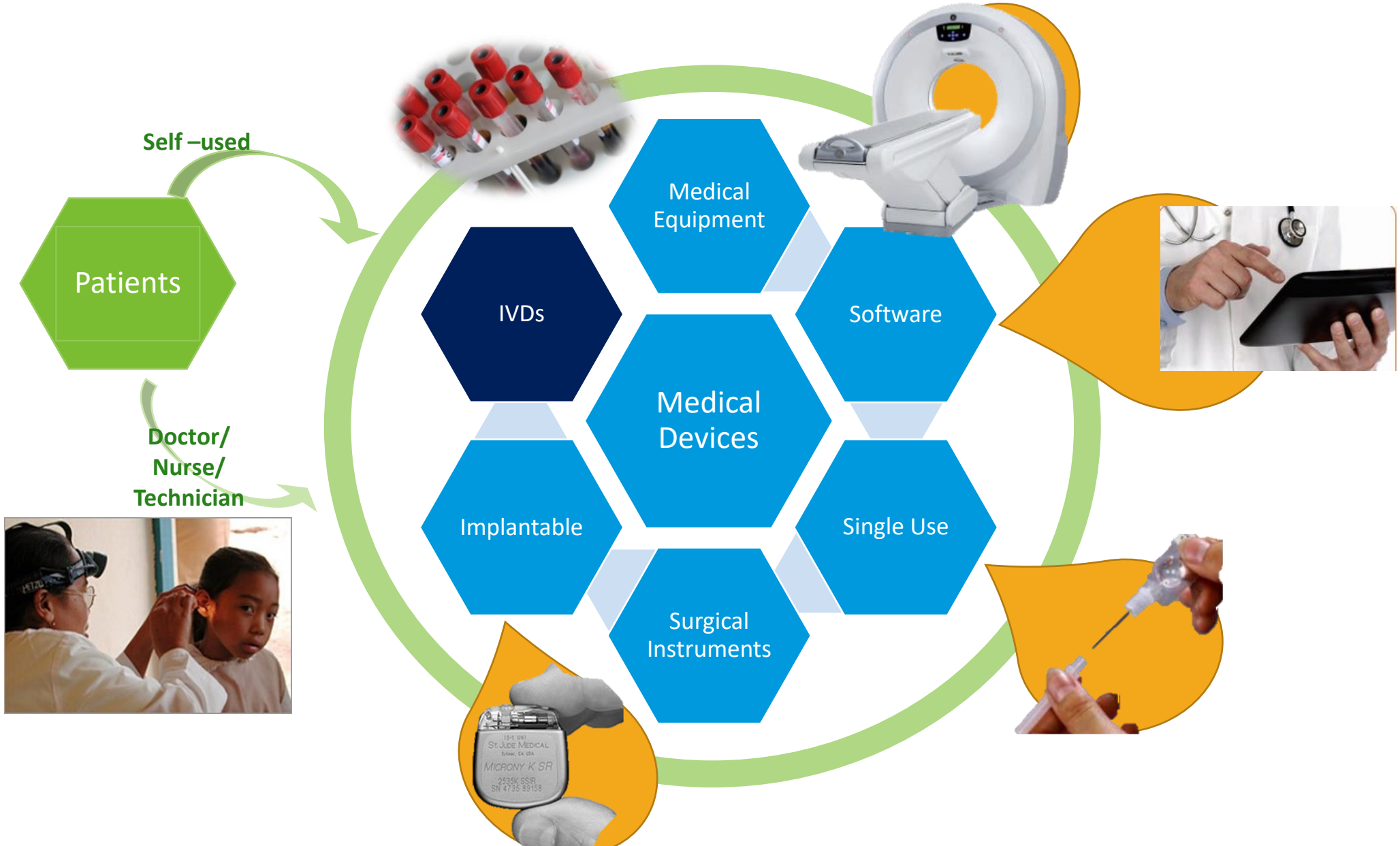
There are thousands of types of Medical devices.
In contrast with medicines: have no pharmacological effects, there are no generics.

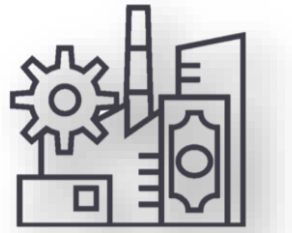


# Value chain: To ensure improved access of safe, quality, affordable, medical devices

Nomenclature

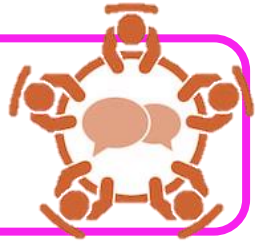
**R&D**

- Industry and Academics: Research and development <u>should be based on needs</u>



**Assessment**

- Health Technology Assessment
- Selection of National Lists of MD for reimbursement or procurement
- **(WHO Essential in vitro Diagnostics and Priority Medical Devices)**



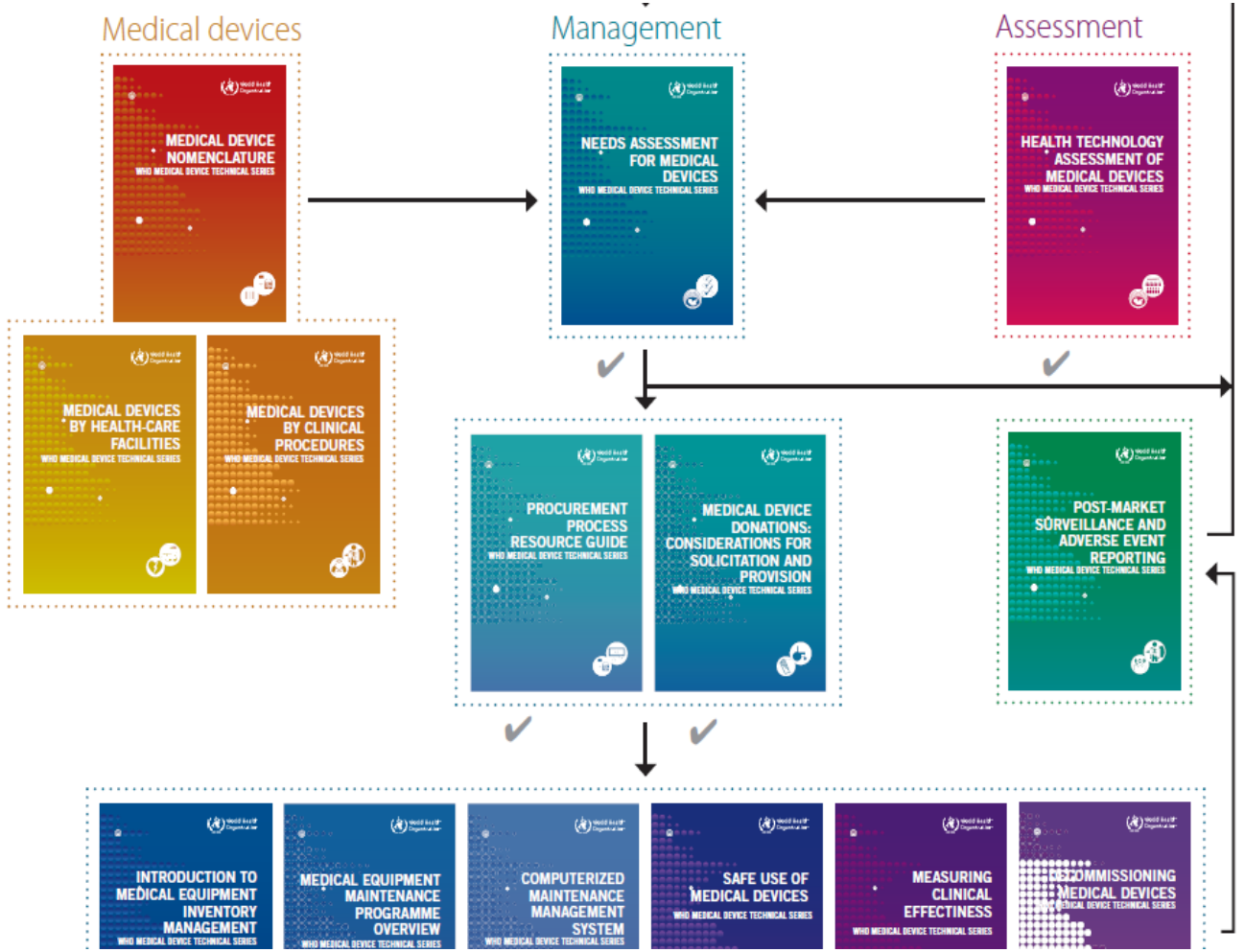
**Regulations**

- Regulation process of medical devices
- Lists of approved MD for marketing in country.

**Management**

- Procurement
- Installation, training, maintenance
- Safe use, operating costs and clinical effectiveness
- Post market surveillance and adverse event report
- Decommissioning, Replacement

# WHO has developed guidance on: HTA, regulation, Health technology management to implement access to priority/essential medical devices.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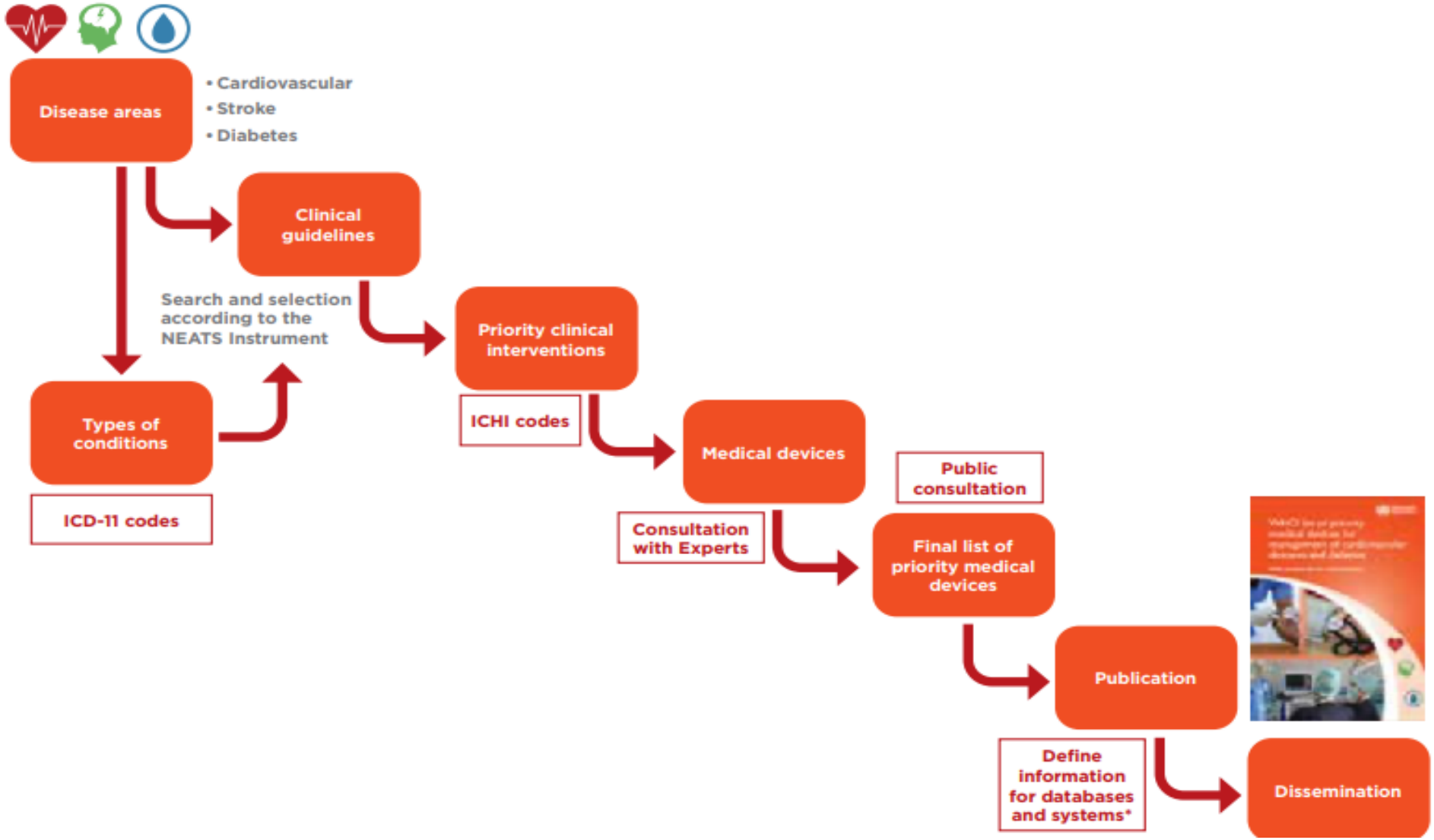
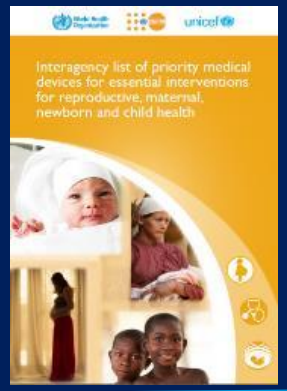
# WHO List of Priority medical devices is evidence based .

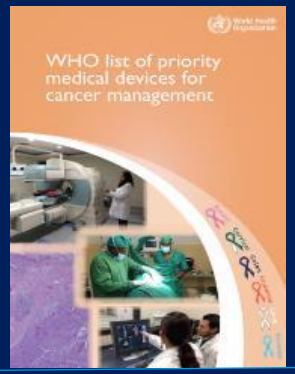


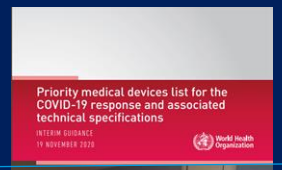
# WHO Priority medical devices

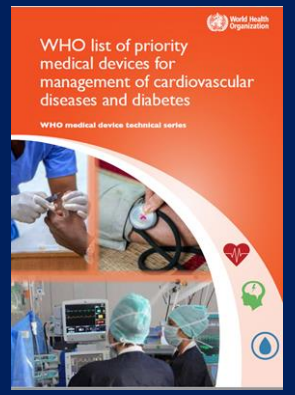
WHO Essential in vitro diagnostics

List of essential/ priority



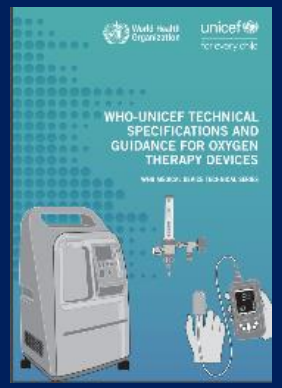



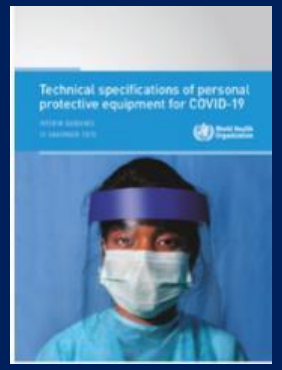



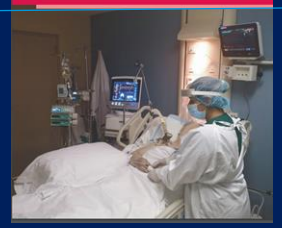



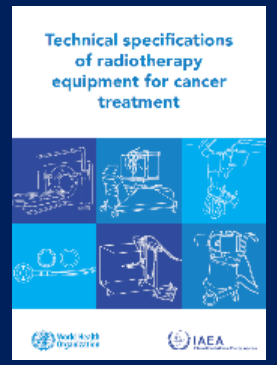


Technical specifications



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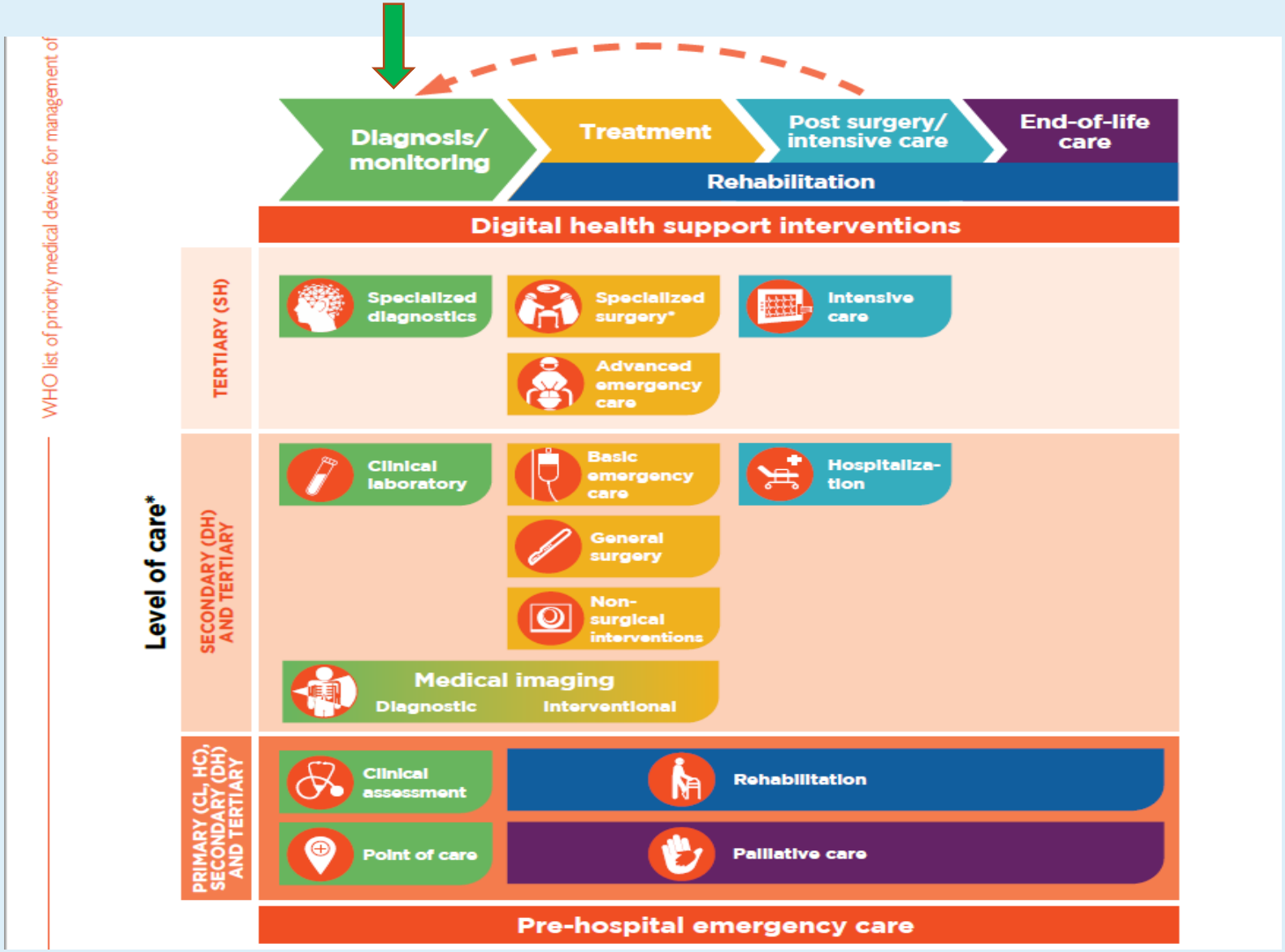
https://www.who.int/health-topics/medical-devices
https://medevis.who-healthtechnologies.org/

Priority Medical Devices can be used for:

Prevention,
**Diagnosis,**
Treatment,
Rehabilitation,
Palliation.

Should be available at different levels of care.

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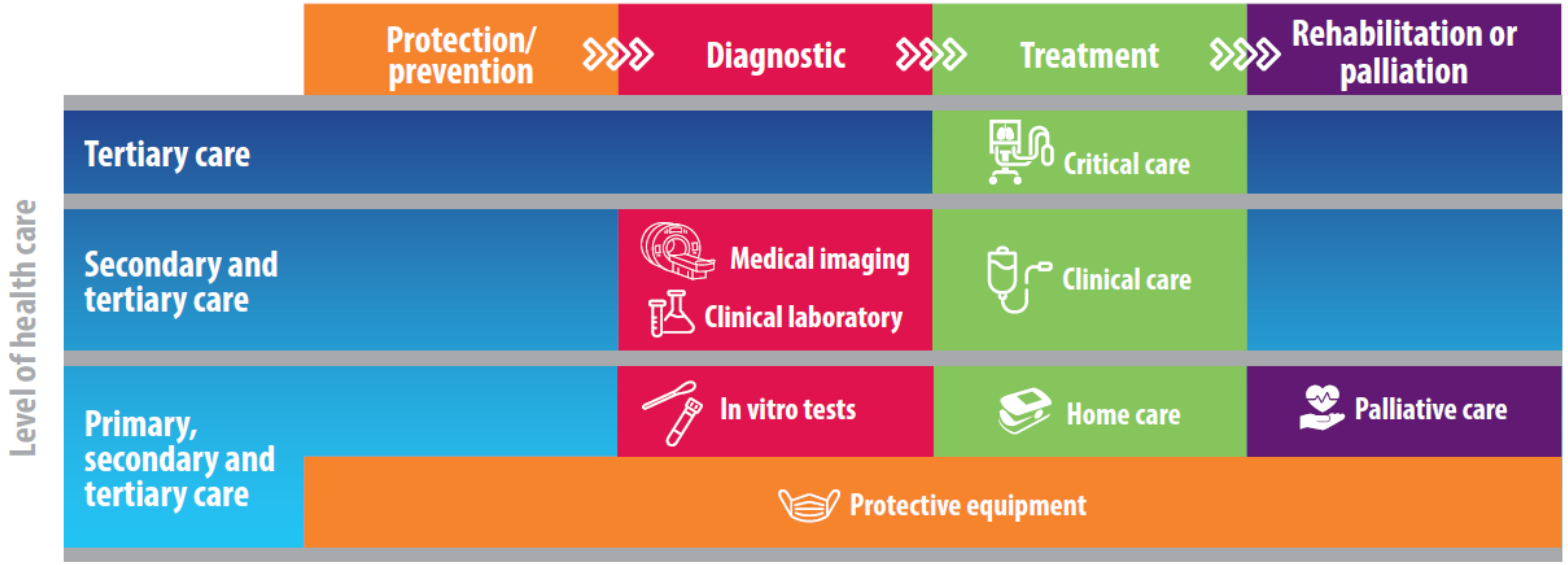
# Medical devices used along the care pathway for COVID-19 response.



## Diagnostic techniques used in human health care can be classified as either

(i) **In vivo techniques**, including:

(ii) medical devices for clinical examination, stethoscopes and blood pressure measurement devices,

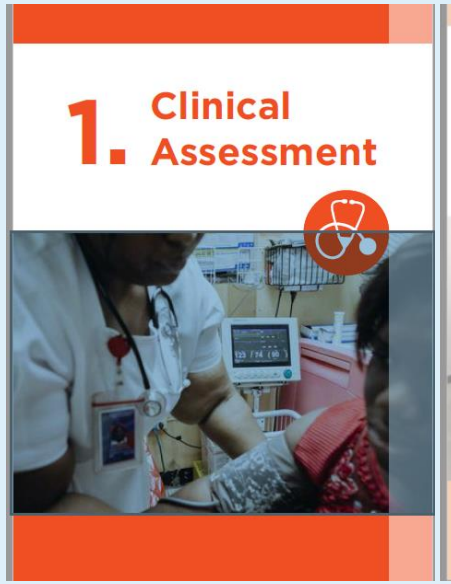
(iii) various types of imaging tests, like ultrasound or computed tomography scanners,

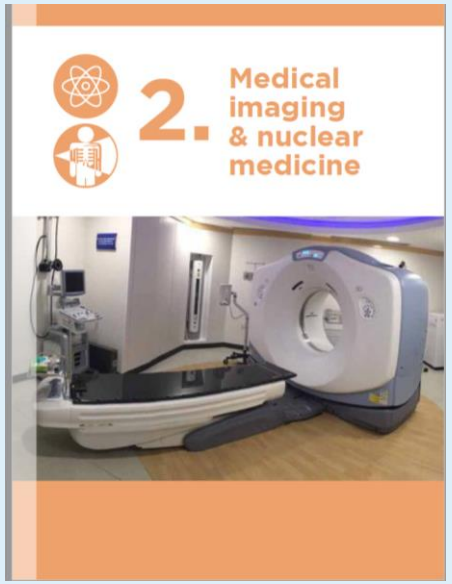
(iv) and electrophysiology, such as electrocardiograms;

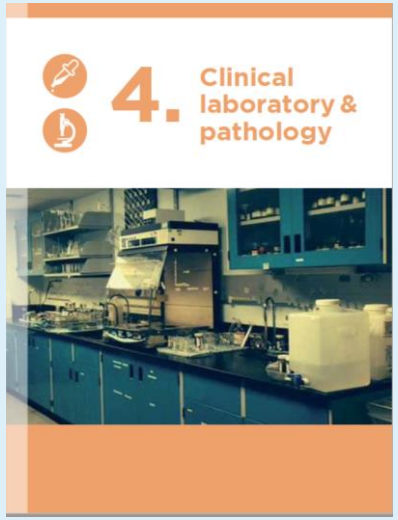
or

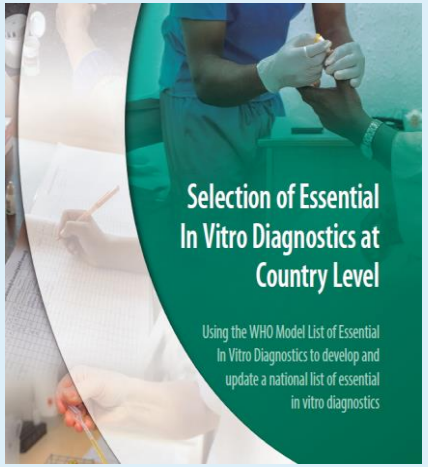
(i) **In vitro tests**, including:

(ii) biochemical, pathology and microbiology tests.

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Source : www.who.int/publications/i/item/9789240030923

# i.e.Interventions require a diagnostic medical device for COVID response

**Table 2.1 Interventions by clinical area**

| Clinical area | Intervention | Triage | Severe patients | Critical patients | 1st level | 2nd level | 3rd level |
|---|---|---|---|---|---|---|---|
| **Clinical assessment** | Body temperature assessment | ● | ● | ● | ● | ● | ● |
| | Oxygen saturation assessment | ● | ● | ● | ● | ● | ● |
| **Medical imaging** | Ultrasound scan | | ● | ● | | ● | ● |
| | CT scan | | ● | ● | | ● | ● |
| | X-ray scan, chest | | ● | ● | | ● | ● |
| **Clinical laboratory** | Blood gas analysis | | ● | ● | | ● | ● |
| | RT-PCR test | ● | ● | ● | ○ | ● | ● |
| | Antigen test | ● | ● | ● | ● | ● | ● |
| **Clinical care** | Multiparametric monitoring | | ● | ● | | ● | ● |

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# Global Implementation:
WHO lists (EDL & PMD) to be used for development or update of national lists, to increase access at country level

- WHO

Review of evidence, guidelines, types of medical devices for interventions

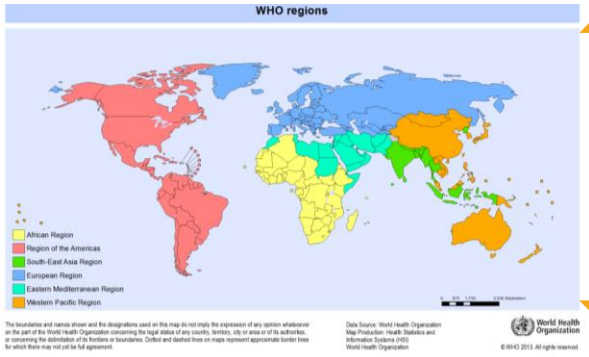
Expert input, Public consultation

Recommendations by SAGE IVD / STAG MEDEV

Publication of list and update e-EDL, MEDEVIS, UHCC, ICD

- Country: National committee

**WHO EDL PMD**




**Prioritized national list**

**Local needs: epidemiology , resources, committee**

- Health facilities. Final users

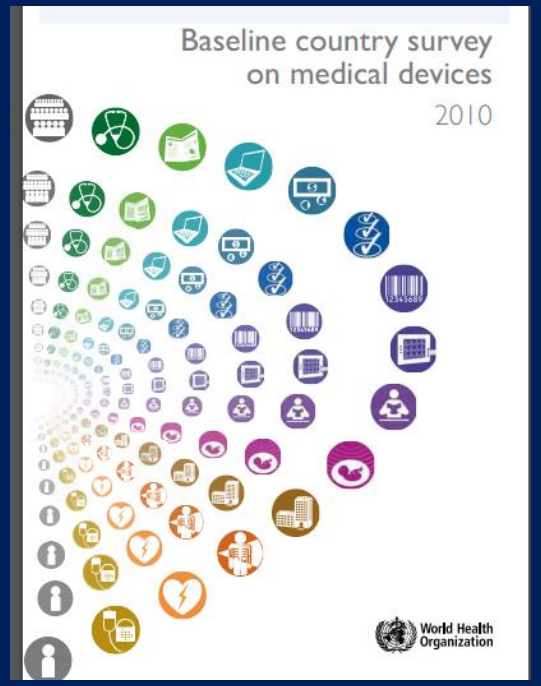
Specialized care, 3rd level

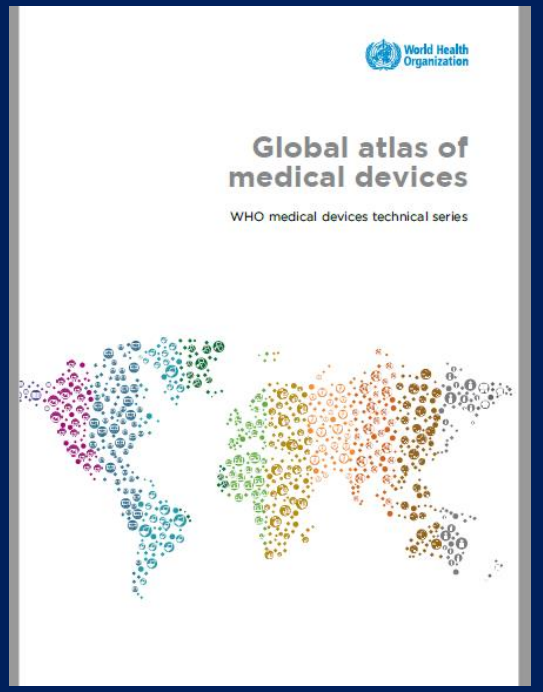
2nd level

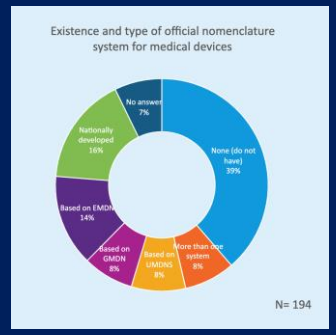
Primary care

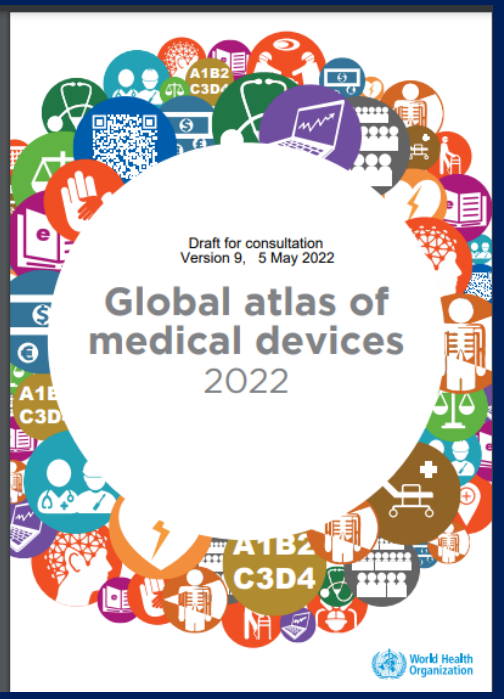
# Global Atlas of Medical devices

- Country profiles
- Data in Global Health Observatory
- Essential or priority national lists per country

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# WHA Mandates

## WHA60.29

- establish and update an evidence web-based health technologies database to serve as a clearinghouse which will provide guidance on appropriate medical devices according to the levels of care, setting and intended health intervention, which can be tailored to the specific needs of country or region”.

## WHA75.25

- to integrate available information related to medical devices, including terms, codes and definitions, in the web-based database and clearinghouse established in line with resolution WHA60.29 (2007) and now available as the Medical Devices Information System (MEDEVIS);3 and to link this to other WHO platforms, such as the International Classification of Diseases (ICD-11),4 to serve as a reference to stakeholders and Member States;

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https://apps.who.int/gb/ebwha/pdf_files/WHA75/A75(25)-en.pdf

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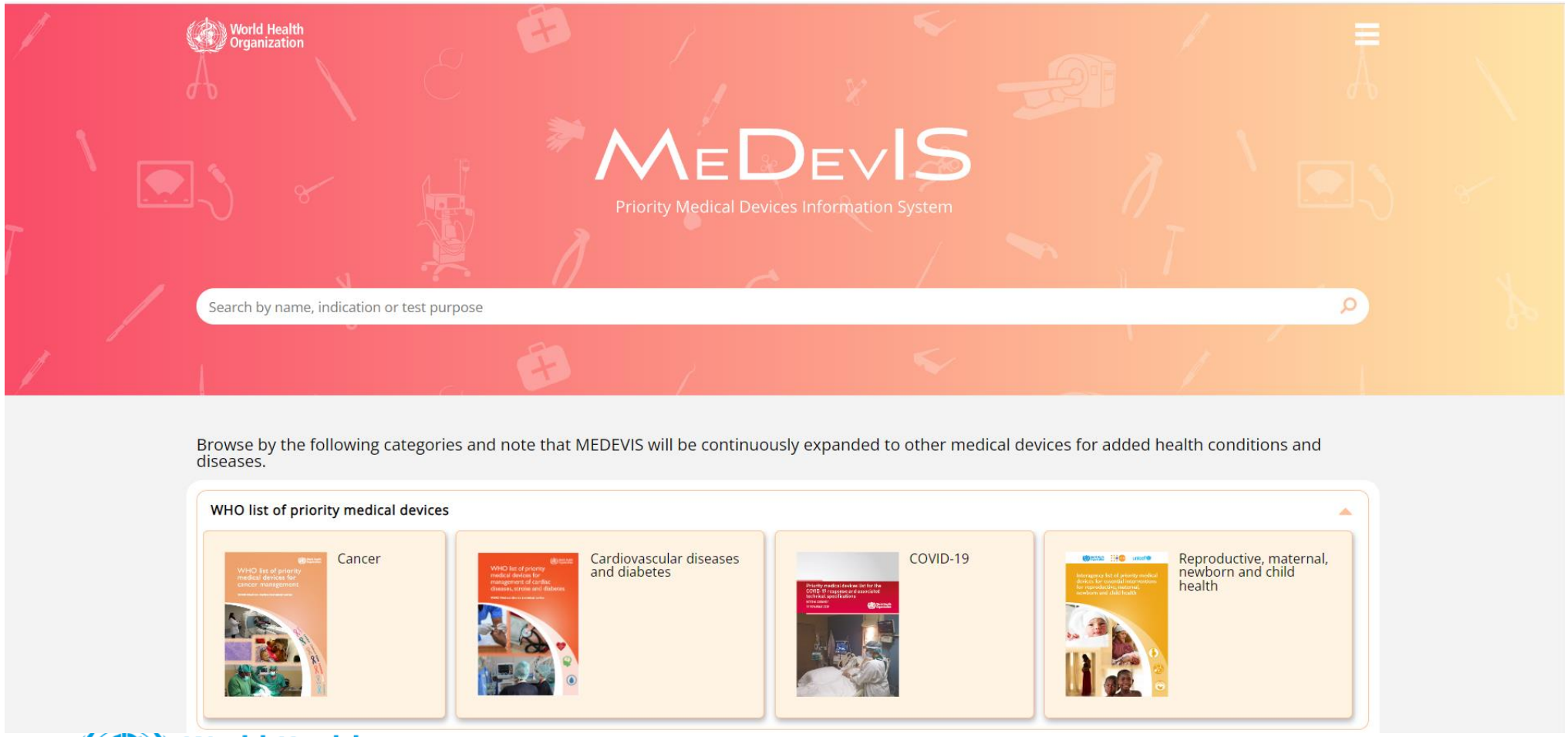
# Medical devices and in vitro diagnostics databases

- WHO Model list of essential in vitro diagnostics (EDL)
- WHO Priority Medical Devices Information System (MeDevIS)

**Other WHO related Lists :**

- Universal Health Coverage Compendium (UHCC) database
- WHO Priority Assistive Products List (WHO APL)
- WHO Model list of Essential Medicines (WHO EML)

# Electronic platform for ease of use:
# WHO Priority medical devices information system **MeDevIS** …

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https://medevis.who-healthtechnologies.org/

https://medevis.who-healthtechnologies.org/devices/COM_321

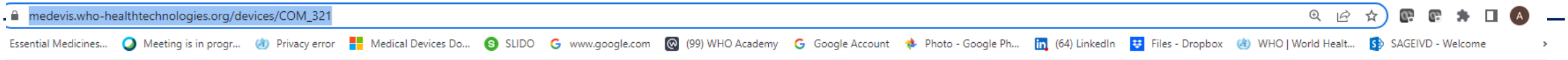
World Health Organization MEDEVIS

Search by name, indication or test purpose

Export device

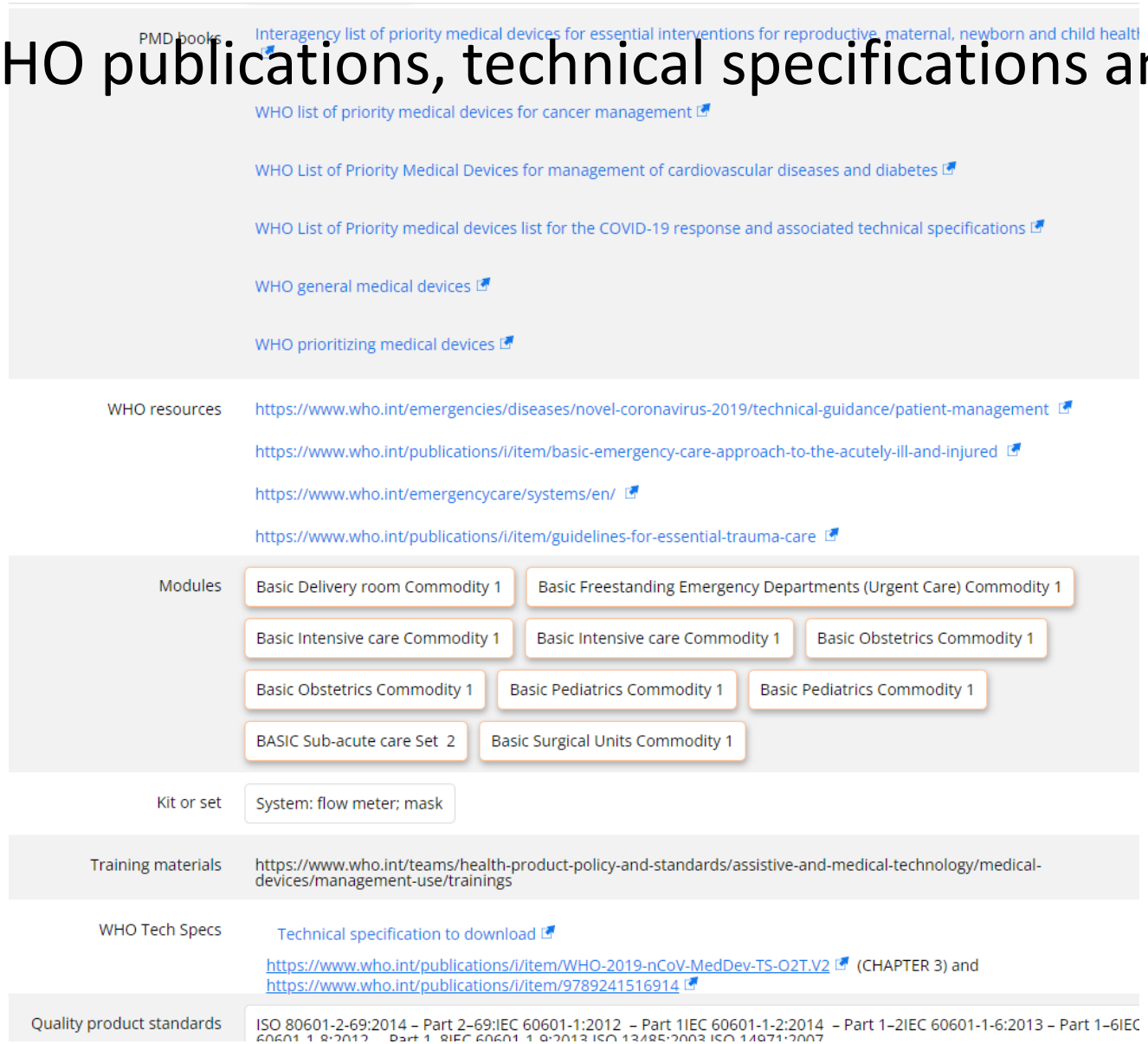
## Oxygen concentrator

| | |
|---|---|
| WHO list of priority medical devices | Cardiovascular diseases and diabetes |
| | COVID-19 |
| | Reproductive, maternal, newborn and child health |
| Various conditions or disease specific | Disease-specific |
| Particular indications (ICD-11) | RA01 COVID-19 |
| | 11 Diseases of the circulatory system |
| | 12 Diseases of the respiratory system |
| | 8B20 Stroke not known if ischaemic or haemorrhagic |



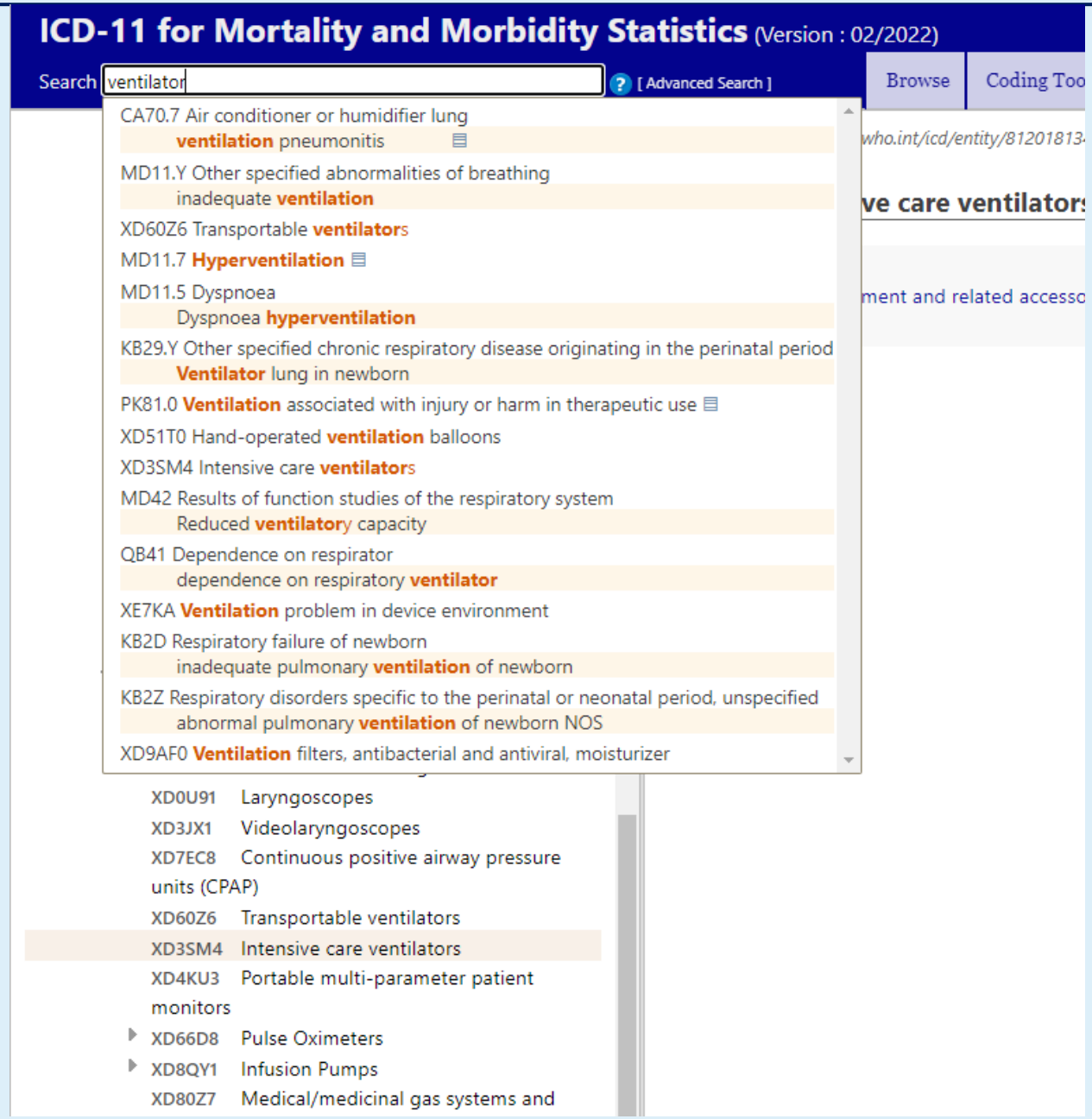

| | |
|---|---|
| Service delivery platforms | 2. Community-based services<br>5. First referral level (District Hospital)<br>6. Second referral level and above (Regional or National hospital) |
| Healthcare unit | Emergency care<br>General surgery<br>Inpatient care<br>Intensive care<br>Long-term care<br>Pre-hospital care<br>Specialized surgery |
| Type of medical device | Medical gas equipment |
| EMDN related* code(s) | Z12159004 OXYGEN CONCENTRATORS<br>https://webgate.ec.europa.eu/dyna2/emdn |
| GMDN related* code(s) | 31321 Mobile/portable oxygen concentrator<br>12873 Stationary oxygen concentrator<br>https://gmdnagency.org<br>© GMDN Agency 2005-2021 |
| UMDNS related* code(s) | 12873 Oxygen Concentrators<br>https://www.ecri.org/solutions/umdns<br>© ECRI. All rights reserved |
| UNSPSC related* code(s) | 42271702 Oxygen concentrators<br>https://store.unspsc.org/collections/codeset-downloads<br>* The codes shown in this section were observed and retrieved from public databases and complemented with the input of Nomenclature Agencies. More information |
| Capital, reusable or single-use | Capital |

# Links to WHO publications, technical specifications and training material, …



| | |
|---|---|
| PMD books | Interagency list of priority medical devices for essential interventions for reproductive, maternal, newborn and child healt<br>WHO list of priority medical devices for cancer management<br>WHO List of Priority Medical Devices for management of cardiovascular diseases and diabetes<br>WHO List of Priority medical devices list for the COVID-19 response and associated technical specifications<br>WHO general medical devices<br>WHO prioritizing medical devices |
| WHO resources | https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/patient-management<br>https://www.who.int/publications/i/item/basic-emergency-care-approach-to-the-acutely-ill-and-injured<br>https://www.who.int/emergencycare/systems/en/<br>https://www.who.int/publications/i/item/guidelines-for-essential-trauma-care |
| Modules | Basic Delivery room Commodity 1<br>Basic Freestanding Emergency Departments (Urgent Care) Commodity 1<br>Basic Intensive care Commodity 1<br>Basic Intensive care Commodity 1<br>Basic Obstetrics Commodity 1<br>Basic Obstetrics Commodity 1<br>Basic Pediatrics Commodity 1<br>Basic Pediatrics Commodity 1<br>BASIC Sub-acute care Set 2<br>Basic Surgical Units Commodity 1 |
| Kit or set | System: flow meter; mask |
| Training materials | https://www.who.int/teams/health-product-policy-and-standards/assistive-and-medical-technology/medical-devices/management-use/trainings |
| WHO Tech Specs | Technical specification to download<br>https://www.who.int/publications/i/item/WHO-2019-nCoV-MedDev-TS-O2T.V2 (CHAPTER 3) and<br>https://www.who.int/publications/i/item/9789241516914 |
| Quality product standards | ISO 80601-2-69:2014 – Part 2–69:IEC 60601-1:2012 – Part 1IEC 60601-1-2:2014 – Part 1–2IEC 60601-1-6:2013 – Part 1–6IEC |

# Links with other WHO platforms ie. ICD-11 relation to diseases, health conditions…

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# Decision approved in WHA 75[1]

28 May 2022

- on standardization of medical devices nomenclature… Decided to request the Director General:

(1)to integrate **available** information related to medical devices, including **terms, codes, and definitions**, in the web-based database and clearinghouse established in line with resolution WHA60.29 (2007) and now available as the Medical Devices Information System (MEDEVIS); and to **link this to other WHO platforms**, such as the International Classification of Diseases, (ICD-11)4 to serve as a reference to stakeholders and Member States;

(2)to submit a substantive report on progress made in implementing this decision to the Executive Board at its 152nd session in January 2023, and **its 15 in January 2025**

https://apps.who.int/gb/ebwha/pdf_files/WHA75/A75(25)-en.pdf



(1) https://apps.who.int/gb/ebwha/pdf_files/WHA75/A75_11Add1-en.pdf

# Way forward

- Medical devices, including In vitro diagnostics are required in all health systems for: emergencies, universal health coverage and wellness.
- They need to be  ensured quality, available, affordable, accessible, safe.
- WHO will continue to develop guidance for MS
- MS to support access to  target population
- The information from the different lists will allow exchange of data for MS and all stakeholders to use.

The final goal is not the technology per se but the effective and promptly diagnosis to patients, to allow treatment accordingly.

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Gracias
Thank you
Merci
Shokran
Xie xie
Spasiva

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# The EDL at country level:
## National EDLs and related IVD activities at regional level

World Health Organization

# SE Asia Region Experience with National Essential Diagnostics Lists

Nov 2022

Stephen Himley MS, MPH
Technical Officer (Health Technologies)
Regional Office for South-East Asia - SEARO

World Health Organization

# Recent experience with NEDLs

- Status of NEDLs in SEA Region (SEAR)
- Some Member States: existing commitment
- Some MS: question NEDL value
- Tools and advocacy messages
- Observations

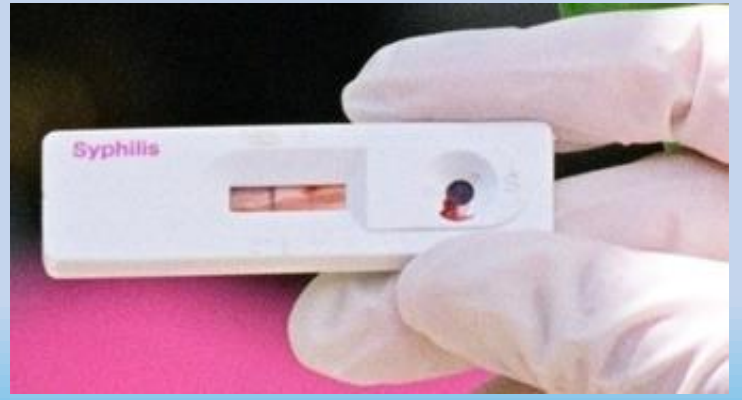
# NEDL status in SEAR

Of 11 Member States:

- India published in 2019
- Timor-Leste active development ongoing
- Nepal draft finalized, in approval process
- Bhutan started planning, requested WHO technical assistance
- Maldives stated intent to start development in 2023
- Indonesia considering

# Timor-Leste: pre-existing commitment

- 2019 National Health Lab scientists discussed after first WHO EDL
- 2021 WHO biennial planning: WCO/MoH request to support NEDL
- 2022 (Mar) SEARO Regional Workshop on Essential Diagnostics
- (May-Sep) WHO consultations with NHL
  - Process, high level support, Technical Working Group (TWG) appointment
- (Sep) WHO hired consultant to assess IVD availability, country needs; draft composite list of IVDs that match / don't match EDL
- (Oct) NEDL development launch, 1st TWG meeting
- Much collaboration: SEARO and TL WHO office



# Other Member States: Advocacy required

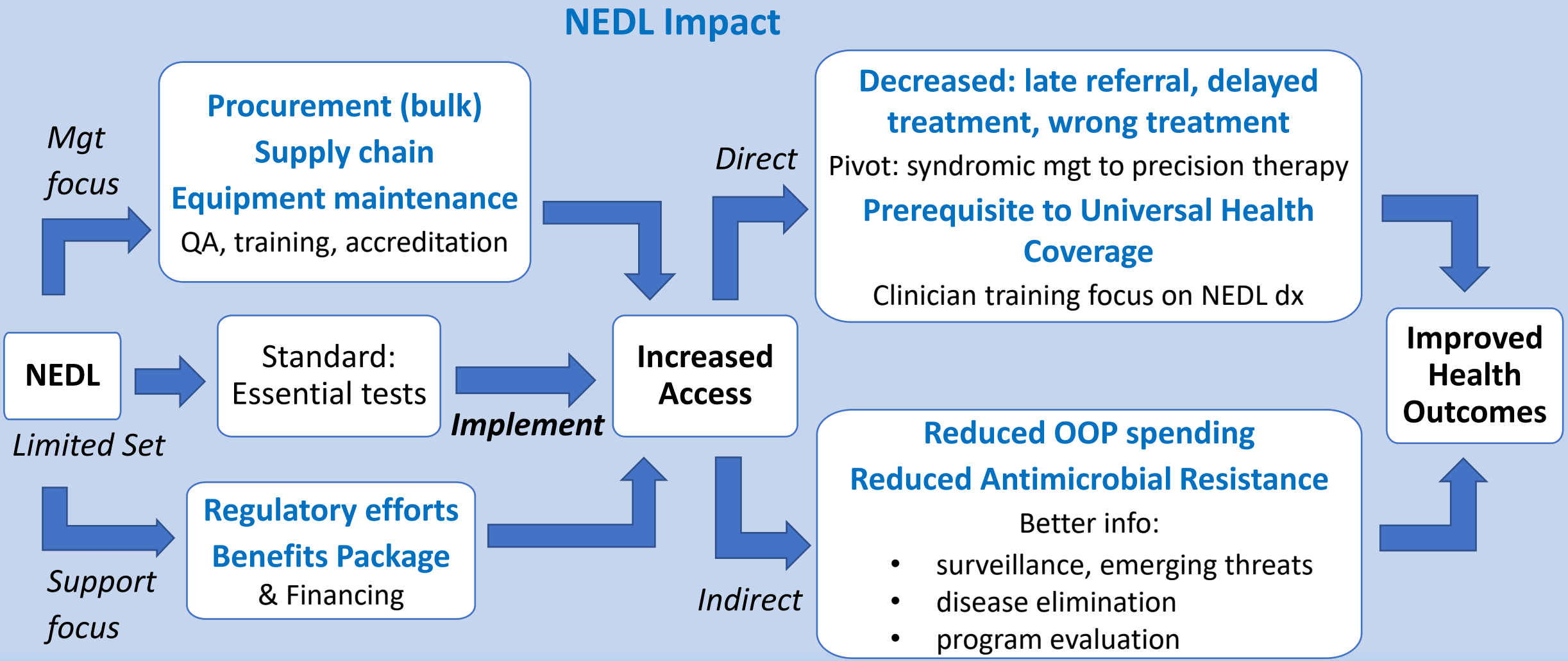
- SEAR MS general request: ↑ access to health technologies
  - Specific response relies on WHO expertise: NEDL
  - “I don’t see why another list is needed”
- Advocacy required: WHO country offices (WCO) and MoH
  - WCO focal points for medical products access – other responsibilities (medicines, health financing, regulatory, …)
- Advocacy efforts:
  - Regional workshop on essential diagnostics
  - WCO medical products focal points meetings
  - Consultations with MoH, organized by WCO

# Advocacy Tools – per MoH / WCO request

- Various PPT presentations
- 1-pager “Importance of NEDL”
- 8-page Concept Note “Development of NEDL”
- TWG guide, example NEDLs, etc.

*Compared to drugs, managing Dx is hard!*

# Associated benefits: crucial for decision



# Some observations

- National Health Lab director typically leads
  - Predominant emphasis on hospital IVDs
  - WHO advocacy for simple diagnostics at PHC level
- Consultant for early heavy lifting quite effective
  - Desk review: IVD availability, disease burden, services packages, …
  - Draft first list organized by IVDs that match and do not match EDL
- Smaller MS: no public call for IVD submissions to NEDL
- Low resource pragmatism
  - IVDs not in EDL: Oral consensus at TWG meetings favored over systematic reviews

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*Thank you*


# EDL and IVD related activities in the Americas

**Alexandre Lemgruber**

Regional Advisor, Health Technologies Management
Unit of Medicines and Health Technologies (HSS/MT)

PAHO Pan American Health Organization
World Health Organization REGIONAL OFFICE FOR THE Americas

# EDL in the Americas

- **First advocacy webinar** to promote the EDL in *September 2022*: *Selection and use of essential in vitro diagnostics* in collaboration with WHO
  - **121 participants** representing **23 countries**
  - Objective: To present and **promote the WHO model list of essential in vitro diagnostics in the Americas** and **share experiences** between countries
  - Topics discussed:
    - WHO model list of essential in vitro diagnostics (EDL), WHO
    - Development of a national essential in vitro diagnostics list, experience from the Ministry of Health, Nigeria
    - Presentation of the report: Access to essential diagnostics in Peru

# EDL in the Americas

- **Translation of the WHO guidance document in Spanish and Portuguese:**

  *Selection of essential in vitro diagnostics at country level: Using the WHO Model List of Essential In Vitro Diagnostics to develop and update a national list of essential in vitro diagnostic*

  - **Spanish version finalized (publication expected: end of 2022)**
  - **Portuguese version in the design phase (publication expected: early 2023)**

# EDL: Next steps

- Dissemination of the guidance document in Spanish and Portuguese through regional networks
- Organization of a webinar to present the guidance document and raise awareness among Member States on the importance of a national essential diagnostics list (NEDL)
- Translation of the next version of the EDL to Spanish and Portuguese (TBD)
- Technical support to Members States, as requested

# Other IVD related activities at the regional level

## Quality assurance for non-WHO-PQ IVDs

- Development of SOPs (on going)
- Collaboration with technical programs

**IVDs requested for procurement**

For example: IVDs for Chagas, Leishmaniasis, Histoplasma, etc.

**Eligibility criteria**

- Part of the third version of the EDL
- Market authorization by SRA or regional members of IMDRF
- Performance evaluation studies

**Technical requirements**

- Regulatory compliance
- Product description
- Post-market surveillance
- Manufacturing information
- Quality management system
- Stability studies
- Etc.

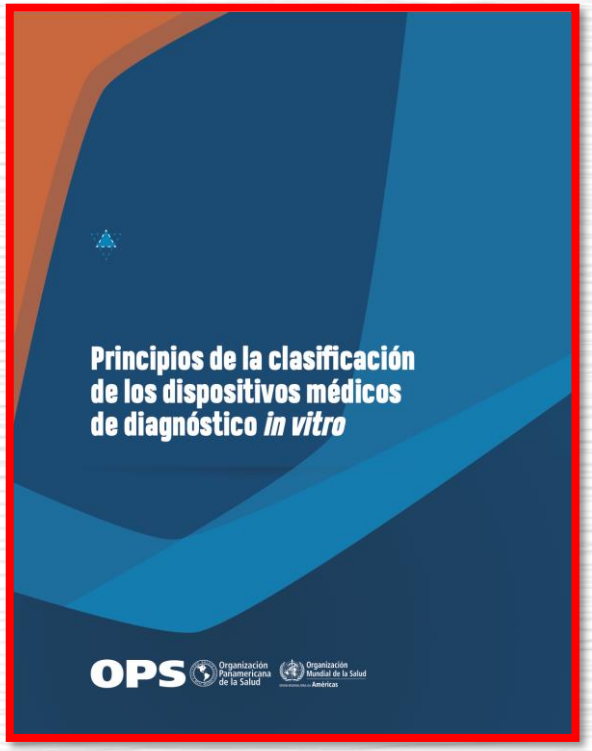
**Assessment of documentation and final decision**

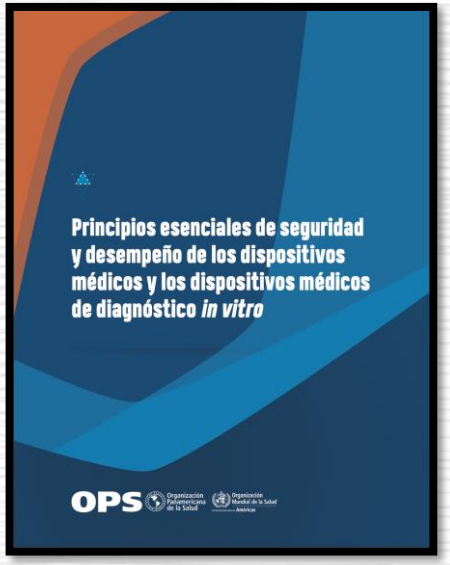
- IVD is eligible or not for procurement

# Other IVD related activities at the regional level

## Collaboration with the International Medical Device Regulators Forum (IMDRF)

- 12 documents translated into Spanish related to medical devices including IVDs
- All documents are available online on PAHO's website




# Other IVD related activities at the regional level

- **Webinars** discussing IVD related topics such as performance evaluation, WHO prequalification process , experience of laboratories in the Americas, Emergency Use Listing (EUL).
- Total of **410 participants** representing **30 countries:**
  1. WHO Emergency Use Listing for IVDs, in collaboration with WHO.
  2. Evaluating Laboratories for WHO Prequalification of IVDs, in collaboration with WHO.
  3. Performance evaluation of In Vitro Diagnostics: Experience of the laboratories in the Region of the Americas.

# Other IVD related activities at the regional level

## Capacity building activity

- Virtual course on postmarket surveillance of In Vitro Diagnostic Medical Devices in Colombia
- In collaboration with INVIMA, the PANDRH Network, and the Regional Working Group on Medical Device Regulation
- One month duration
- Content
  - Unit 1. General overview
  - Unit 2. National Program for IVD surveillance
  - Unit 3. Clinical Risk Management System
  - Unit 4. Application of the FMEA Methodology
  - Unit 5. Use of the web application

Registration will start soon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# Thank you!

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# Q&A session

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# Thank you

For more information on the EDL, please contact us at
EDLsecretariat@who.int

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