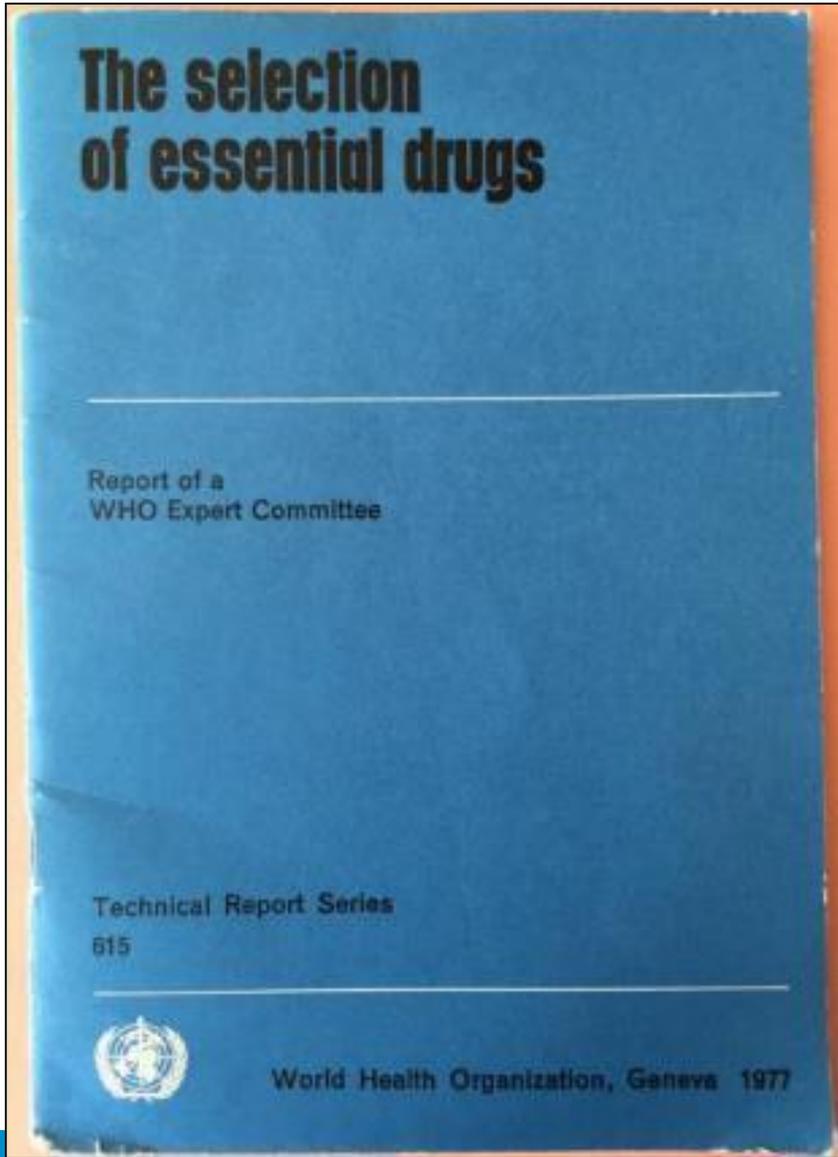


WHO EML Antibiotic Working Group. Building **A**W**a**R**e**-ness

Professor Mike Sharland
Chair of the AB WG
St George's University London



1977

First Model EML

- 16 antibiotics
(of 240 medicines ≈ 7%)

First EML children 2007

In a report¹ to the Twenty-eighth World Health Assembly in 1975, the Director-General reviewed the main drug problems facing the developing countries and outlined possible new drug policies. The Director-General also referred to the experience gained in some countries where schemes of basic or essential drugs had been implemented. Such schemes were intended to extend the accessibility of the most necessary drugs to those populations whose basic health needs could not be met by the existing supply system. The Director-General pointed out that the selection of these essential drugs would depend on the health needs and on the structure and development of health services of each country, and that lists of essential drugs should be drawn up locally, and periodically updated, with the advice of experts in public health, medicine, pharmacology, pharmacy and drug management. He also considered that adequate information on the properties, indications and use of the drugs listed should be provided. By resolution WHA28.66, the Health Assembly requested the Director-General to implement the proposals contained in his report and, in particular, to advise Member States on the selection and procurement, at reasonable cost, of essential drugs of established quality corresponding to their national health needs.

Antibacterial drugs

- ampicillin (1) *
- benzathine benzylpenicillin (5) *
- benzylpenicillin *

- chloramphenicol (7) *
- cloxacillin (penicillinase-resistant, 1) *
- erythromycin *
- gentamicin (4) *
- phenoxymethylpenicillin *
- salazosulfapyridine
- sulfadimidine (1)
- sulfamethoxazole + trimethoprim *
- tetracycline (1, 4) *

Complementary

- amikacin (1, 4, 10)*
- doxycycline (6, 5) *
- procaine benzylpenicillin (7) *
- sulfadiazine (7, 8) *

* On 2021 EML/c

Following the AMR Global Action Plan, in 2017 WHO EML AB WG set up to review AB listing on the EML (geographically representative and gender balanced).

The AB WG developed the **AWaRe** classification of Essential Antibiotics on the EML/c as a simple method to improve stewardship and monitoring.

A-CCESS group: narrow spectrum, safe, affordable antibiotics widely available.

Wa-TCH group: broader spectrum antibiotics used for specific and limited indications due to higher resistance and toxicity potential.

Re-SERVE group: last resort antibiotics that should be used only for treatment of multi-resistant bacteria.

“EML - WHAT ANTIBIOTICS TO USE”

Access	
• Amikacin	• Cloxacillin
• Amoxicillin	• Doxycycline
• Ampicillin	• Gentamicin
• Amoxicillin–clavulanic acid	• Metronidazole
• Benzathine benzylpenicillin	• Nitrofurantoin
• Benzylpenicillin	• Phenoxymethyl penicillin
• Cefazolin	• Procaine penicillin
• Chloramphenicol	• Spectinomycin
• Clindamycin	• Sulfamethoxazole–trimethoprim

Watch	
• Azithromycin	• Vancomycin (intravenous* and oral)
• Cefixime	• Ciprofloxacin
• Ceftriaxone	• Clarithromycin
• Cefotaxime	• Meropenem*
• Ceftazidime*	• Piperacillin–tazobactam
• Cefuroxime	

Reserve*	
• Fosfomycin (intravenous)	• Ceftazidime–avibactam
• Linezolid	• Meropenem–vaborbactam
• Colistin	• Plazomicin
• Polymyxin B	

- **2019 EC** expanded the **AWaRe** classification to over **200 antibiotics not on the EML**
- A new category of **Not Recommended** was added – mainly inappropriate Fixed-Dose Combinations of multiple broad-spectrum antibiotics.
- **WHO 13th General Programme of Work (GPW)** included a Target indicator that at least 60% of total antibiotic use at a country level should be **Access** antibiotics.

2021

World Health Organization Model List of Essential Medicines

22nd List
(2021)



22nd EML

- 39 antibiotics
 - (8th EMLc - 36)
- (of 479 medicines ≈ 8%)

ACCESS
GROUP

WATCH
GROUP

RESERVE
GROUP

Amikacin	Azithromycin
Amoxicillin	Cefixime
Amoxicillin/clavulanic-acid	Cefotaxime
Ampicillin	Ceftazidime
Benzathine-benzylpenicillin	Ceftriaxone
Benzylpenicillin	Cefuroxime
Cefalexin	Ciprofloxacin
Cefazolin	Clarithromycin
Chloramphenicol	Meropenem
Clindamycin	Piperacillin/tazobactam
Cloxacillin	Vancomycin (IV)
Doxycycline	Vancomycin (oral)
Gentamicin	Cefiderocol
Metronidazole	Ceftazidime/avibactam
Nitrofurantoin	Colistin (IV)
Phenoxymethylpenicillin	Fosfomicin (IV)
Procaine-benzylpenicillin	Linezolid
Spectinomycin	Meropenem/vaborbactam
Sulfamethoxazole/TMP	Plazomicin
Trimethoprim	Polymyxin B (IV)

SIXTY-EIGHTH WORLD HEALTH ASSEMBLY

WHA68.7

Agenda item 15.1

26 May 2015

Global action plan on antimicrobial resistance

The Sixty-eighth World Health Assembly,

Having considered the summary report on progress made in implementing resolution WHA67.25 on antimicrobial resistance and the report on the draft global action plan on antimicrobial resistance;¹

Recalling resolutions WHA39.27 and WHA47.13 on the rational use of drugs, resolution WHA51.17 on emerging and other communicable diseases: antimicrobial resistance, resolution WHA54.14 on global health security: epidemic alert and response, resolution WHA58.27 on improving the containment of antimicrobial resistance, resolution WHA60.16 on progress in the rational use of medicines and resolution WHA66.22 on follow up of the report of the Consultative Expert Working Group on Research and Development: Financing and Coordination and WHA67.25 on antimicrobial resistance;

WHO Access, Watch, Reserve (AWaRe) classification of antibiotics for evaluation and monitoring of use, 2021

To assist in the development of tools for antibiotic stewardship at local, national and global levels and to reduce antimicrobial resistance, the Access, Watch, Reserve (AWaRe) classification of antibiotics was developed – where antibiotics are classified into different groups to emphasize the importance of their appropriate use. This classification is intended to be used as a tool for countries to better support antibiotic monitoring and stewardship activities. It is not intended as model for the inclusion of antibiotics on national essential medicine lists. Antibiotics classified under AWaRe and also included on the WHO Model Lists of Essential Medicines are indicated in the worksheets.

Antibiotic	Class	ATC code	Category	Listed on EML/EMLc 2021
Amikacin	Aminoglycosides	J01GB06	Access	Yes
Amoxicillin	Penicillins	J01CA04	Access	Yes
Amoxicillin/clavulanic-acid	Beta-lactam/beta-lactamase-inhibitor	J01CR02	Access	Yes
Ampicillin	Penicillins	J01CA01	Access	Yes
Ampicillin/sulbactam	Beta-lactam/beta-lactamase-inhibitor	J01CR01	Access	No
Arbekacin	Aminoglycosides	J01GB12	Watch	No
Aspoxicillin	Penicillins	J01CA19	Watch	No
Azidocillin	Penicillins	J01CE04	Access	No
Azithromycin	Macrolides	J01FA10	Watch	Yes
Azlocillin	Penicillins	J01CA09	Watch	No
Aztreonam	Monobactams	J01DF01	Reserve	No
Bacampicillin	Penicillins	J01CA06	Access	No
Bekanamycin	Aminoglycosides	J01GB13	Watch	No
Benzathine-benzylpenicillin	Penicillins	J01CE08	Access	Yes
Benzylpenicillin	Penicillins	J01CE01	Access	Yes
Biapenem	Carbapenems	J01DH05	Watch	No
Brodiprim	Trimethoprim-derivatives	J01EA02	Access	No
Carbenicillin	Penicillins	J01CA03	Watch	No
Carindacillin	Penicillins	J01CA05	Watch	No
Carumonam	Monobactams	J01DF02	Reserve	No
Cefacetrile	First-generation-cephalosporins	J01DB10	Access	No
Cefaclor	Second-generation-cephalosporins	J01DC04	Watch	No
Cefadroxil	First-generation-cephalosporins	J01DB05	Access	No
Cefalexin	First-generation-cephalosporins	J01DB01	Access	Yes
Cefaloridine	First-generation-cephalosporins	J01DB02	Access	No
Cefalotin	First-generation-cephalosporins	J01DB03	Access	No
Cefamandole	Second-generation-cephalosporins	J01DC03	Watch	No
Cefepim	First-generation-cephalosporins	J01DB08	Access	No

257 Antibiotics have an AWaRe group
 39 on EML
 Around 100 Not Recommended

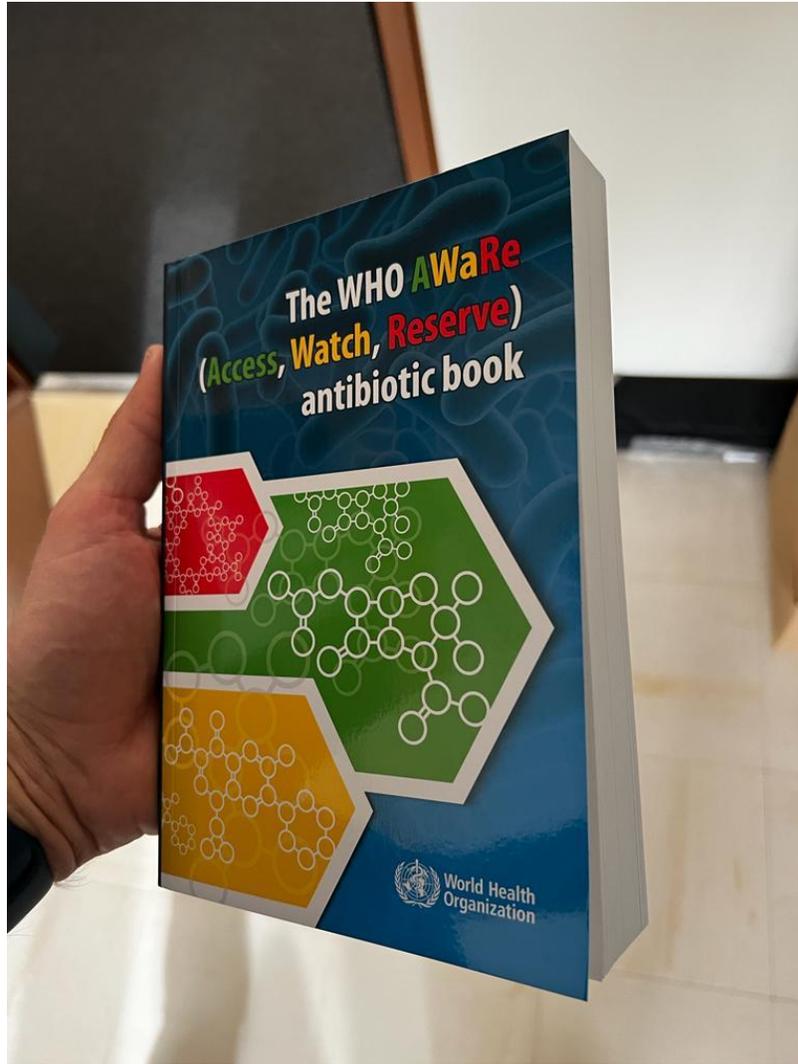
WHO EML Antibiotic AWaRe Book (2022)

- Now provides simple guidance on “HOW TO USE the antibiotics on the EML to manage most common infections
- Guidance for 34 infections; primary care and facility/hospital setting, children and adults.
 - acute bacterial infections (Not TB/viral/fungal/parasitic infections)
 - **Recommendations on empiric antibiotic treatment** (i.e. presumptive diagnosis not requiring any laboratory diagnostic)
 - Includes guidance on making the clinical Diagnosis, the Decision if antibiotic needed, the choice of Drug, Dose, Duration
 - Developed in close collaboration with the WHO Division of AMR (GLASS/ASP) and many other departments
 - Short educational summaries of key features of microbiology, epidemiology, clinical presentation, diagnostics, prevention
 - **Target audience: all health professionals giving antibiotics**

General principles of AWaRe Book

- **Goals of improving clinical care and optimise the use of narrow spectrum **Access** antibiotics (especially in Primary Care)**
- Provide guidance on **Symptomatic care** and **when to prescribe/not prescribe** using a risk-based approach (mild/severe symptoms; ill/not ill; underlying disease such as HIV/malnutrition/no underlying disease)
- Guidance regarding diagnostics was given where there was a **clear evidence base** for their added utility (choice of tests based on collaboration with the **WHO EDL**)
- Standardisation of guidance for essential drug/dose/duration/formulation across infections to simplify future implementation and allow monitoring of the availability in pharmacies of quality and affordable medicines.
- **Guidance varied based on different rates of AMR for common infections assessed using GLASS data**
- **Reserve antibiotics – criteria for selection and stewardship, short drug summaries and guidance on when to use specific drugs in relevant infections – linked to WHO AB Pipeline and Priority Pathogen List**
- Primary and secondary care focussed stewardship goals – closely aligned to WHO ASP Toolkit and WHO Policy Guidance on Integrated Stewardship Activities
- **Book designed to support the use of the AWaRe system as a quality improvement tool (and assist with developing policy goals)**

Implementation focussed design



World Health Organization **CHILDREN**

Community-Acquired Pneumonia

Page 2 of 2

Severity Assessment and Considerations

Children with pneumonia:

- Should be treated with oral amoxicillin at home with home care advice
- Pneumonia is diagnosed on either:
 - Fast breathing (respiratory rate > 50 breaths/minute in children aged 2-11 months; resp rate > 40 breaths/min in children aged 1-5 years)
 - Chest indrawing

Children with severe pneumonia (or a child with pneumonia who cannot tolerate oral antibiotics):

- Should be admitted to hospital and treated with intravenous antibiotics
- Severe pneumonia is diagnosed on either:
 - A cough or difficulty in breathing plus one of:
 - Oxygen saturation below 90%
 - Central cyanosis
 - Severe respiratory distress (e.g. grunting or severe chest indrawing)
 - Signs of pneumonia with a general danger sign:
 - Inability to drink or breast feed
 - Persistent vomiting
 - Convulsions
 - Lethargy or unconsciousness
 - Severe respiratory distress

Antibiotic Treatment Duration

Treat for 5 days

If severe disease, consider longer treatment and look for complications such as empyema, if patient not clinically stable at day 5

Mild to Moderate Cases

All dosages are for normal renal function

Amoxicillin 40-50 mg/kg/dose q12h ORAL

Oral weight bands:

3-6 kg	125 mg q12h
6-10 kg	250 mg q12h
10-15 kg	500 mg q12h
15-20 kg	750 mg q12h
20-30 kg	1000 mg q12h
≥30 kg	Use adult dose

Treatment

Severe Cases

Please see Severity Assessment and Considerations for diagnosis of severe cases

All dosages are for normal renal function

First Choice

Amoxicillin 50 mg/kg/dose IV/IM
 • ≤1wk of life: q12h
 • >1wk of life: q8h

OR

Amoxicillin 50 mg/kg/dose IV/IM
 • ≤1wk of life: q12h
 • >1wk of life: q8h

OR

Benzylopenicillin 30 mg/kg (50 000 IU/kg) q8h IV

COMBINED WITH

Gentamicin IV/IM
 • Neonates: 5 mg/kg/dose q24h
 • Children: 7.5 mg/kg/dose q24h

IF HIV POSITIVE AND <1 YR OLD
 To treat potential Pneumocystis jirovecii pneumonia, ADD

Sulfamethoxazole-trimethoprim 40 mg/kg SMX+8 mg/kg TMP q8h IV/ORAL for 3 weeks

Second Choice

If NO Clinical Response to First Choice after 48-72 hours

Cefotaxime 50 mg/kg/dose q8h IV/IM

OR

Ceftriaxone 80 mg/kg/dose q24h IV/IM

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The WHO AWaRe (Access, Watch, Reserve) antibiotic book and prevention of antimicrobial resistance

Veronica Zanichelli,^a Michael Sharland,^b Bernadette Cappello,^a Lorenzo Moja,^a Haileyesus Getahun,^c Carmem Pessoa-Silva,^d Hatim Sati,^c Catharina van Weezenbeek,^d Hanan Balkhy,^e Mariângela Simão,^f Sumanth Gandra^g & Benedikt Huttner^a

Abstract Guidance on the appropriate use of antibiotics for common infections is lacking in many settings. The World Health Organization (WHO) has recently released *The WHO AWaRe (Access, Watch, Reserve) antibiotic book* which complements the *WHO Model list of essential medicines* and *WHO Model list of essential medicines for children*. The book gives specific guidance on the empiric use of antibiotics in the model lists with a strong emphasis on the AWaRe framework, which is centred around the risk of antimicrobial resistance development associated with the use of different antibiotics. Recommendations in the book cover 34 common infections in primary and hospital care both for children and adults. The book also includes a section on the use of the last-resort Reserve antibiotics, whose use should be restricted to very selected cases when an infection is confirmed or suspected to be caused by multidrug-resistant pathogens. The book highlights the use of first-line Access antibiotics or no antibiotic care if this is the safest approach for the patient. Here we present the background behind the development of the AWaRe book and the evidence behind its recommendations. We also outline how the book could be used in different settings to help reach the WHO target of increasing the proportion of global consumption of Access antibiotics to at least 60% of total consumption. The guidance in the book will also more broadly contribute to improving universal health coverage.

WHO AWaRe

- Book is a new step for the EML, it has taken nearly 50 years for the “List” of antibiotics to evolve into guidance on optimal “Use”.
- The AWaRe system has been developed to improve the quality of global AB use (over 90% are oral generic antibiotics taken in primary care – Book recommends nearly all should be Access antibiotics; high over-use globally of oral broad-spectrum Watch antibiotics)
- Helping to build the evidence for the sustainable use and access to essential Access antibiotics (SDG 3.8 - safe, effective, quality and affordable medicines) and assist with defining measurable impacts of UHC and Triple Billion Target.
- Now significant work on refining and implementing AWaRe
- Thank all members of the WHO EML Secretariat, AB WG, AMR Division, responders to public consultation and all other internal and external collaborators