A GLOBAL COMMITMENT

SUSTAINABLE DEVELOPMENT GOAL (SDG) 3

“Ensure healthy lives and promote well-being for all at all ages”

“Achieve Universal Health Coverage...access to safe, effective, quality, and affordable essential medicines and vaccines for all”
WHO GLOBAL PROGRAMME OF WORK
GPW 13

HEALTH EMERGENCIES
1 billion more people better protected from health emergencies

HEALTHIER POPULATIONS
1 billion more people enjoying better health & well-being

UNIVERSAL HEALTH COVERAGE
1 billion more people benefiting from health coverage
ACCESS TO MEDICINES, VACCINES AND HEALTH PRODUCTS

AFFORDABLE
EFFECTIVE
QUALITY-ASSURED
SAFE
AFFORDABILITY
BARRIERS PERSIST IN MANY DEVELOPING COUNTRIES

- 90% of the population pays for medicines out-of-pocket.
- 100 million people are driven into poverty every year.
- Medicines represent the LARGEST family expenditure after food.
- On average, a family in Tanzania spends 53% of family income to treat a child with type-1 diabetes.
CHALLENGES have expanded to DEVELOPED COUNTRIES

Latest treatments for cancer and hepatitis C

e.g. USA 2015 - average prices for new cancer drugs US$ 7 500 to US$ 28 000 per month

Orphan drugs for rare diseases

Insulin (discovered in 1923) - cost up to US$ 340

Need for balance between R&D costs and final price – a “FAIR PRICE”
PRICES OF DRUGS TO CURE HEPATITIS C 
BY COUNTRY - SOFOSBUVIR PLUS DACLATASVIR

<table>
<thead>
<tr>
<th>Country</th>
<th>Price of a 12-week course in USD</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA (Nadac)</td>
<td>$142,710</td>
</tr>
<tr>
<td>DENMARK</td>
<td>$104,723</td>
</tr>
<tr>
<td>USA (Veteran)</td>
<td>$96,404</td>
</tr>
<tr>
<td>NORWAY</td>
<td>$87,632</td>
</tr>
<tr>
<td>GERMANY</td>
<td>$84,281</td>
</tr>
<tr>
<td>UNITED KINGDOM</td>
<td>$76,757</td>
</tr>
<tr>
<td>CANADA (Quebec)</td>
<td>$68,280</td>
</tr>
<tr>
<td>SWEDEN</td>
<td>$65,616</td>
</tr>
<tr>
<td>FRANCE</td>
<td>$50,059</td>
</tr>
<tr>
<td>ARGENTINA</td>
<td>$47,972</td>
</tr>
<tr>
<td>SAUDI ARABIA</td>
<td>$37,729</td>
</tr>
<tr>
<td>SPAIN</td>
<td>$33,800</td>
</tr>
<tr>
<td>BRAZIL</td>
<td>$29,361</td>
</tr>
<tr>
<td>AUSTRALIA</td>
<td>$5,540</td>
</tr>
<tr>
<td>THAILAND</td>
<td>$9,906</td>
</tr>
<tr>
<td>EGYPT</td>
<td>$84</td>
</tr>
<tr>
<td>INDIA</td>
<td>$78</td>
</tr>
</tbody>
</table>

Estimated: $47

From a presentation from Andrew Hill, Feb 2018
No public sector or health insurance system can afford to supply or reimburse every available medicine or health technology

- Need for systems to facilitate selection - improve supply and access, rational prescribing and control costs

**WHO Essential Medicines List (EML)** - selection of medicines that offer the best payback in terms of benefits to patients – since 1978

**Essential Diagnostics List - 2018**
EML WORKING GROUP ON CANCER MEDICINES

75% of drugs approved in the last 15-20 years lacked evidence of substantial clinical benefit at registration.

48 cancer medicines approved by the EMA between 2009 and 2013 for use in 68 different indications:

57% of approved indications, evidence from trials showed no benefits for either survival or quality of life.

CONCLUSIONS FROM MANY ARTICLES

Prices for some new and innovative medicines do not necessarily reflect an increase in benefits provided to patients.
### WHO ANTIBIOTIC AWARE LIST

<table>
<thead>
<tr>
<th><strong>KEY ACCESS</strong></th>
<th><strong>WATCH GROUP</strong></th>
<th><strong>RESERVE</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>First or second choice antibiotics</td>
<td>Have higher resistance potential</td>
<td>Should be treated as “last resort” options</td>
</tr>
<tr>
<td>Should be widely available, affordable and quality-assured</td>
<td>Key targets of stewardship programs and monitoring</td>
<td>Tailored to highly specific patients and settings, when all alternatives have failed</td>
</tr>
<tr>
<td>Most frequently reported API: amoxicillin, penicillin, sulfamethoxazole, cloxacillin…</td>
<td>Most frequently reported API: ciprofloxacin, ceftriaxone, clarithromycin, ceftazidime…</td>
<td>Reported products: Linezolid</td>
</tr>
</tbody>
</table>

- **77%** of antibiotics in the database are Key Access antibiotics
- **18%** of antibiotics in the database are on the Watch Group
- **2** reports in the GSMS database of reserve group antibiotics

* WHO Essential Medicines List

Data extracted 11 January 2018
Misuse of ANTIBIOTICS puts us all at risk.

Taking antibiotics when you don’t need them speeds up antibiotic resistance. Antibiotic resistant infections are more complex and harder to treat. They can affect anyone, of any age, in any country.

Always seek the advice of a healthcare professional before taking antibiotics.
REGULATORY SYSTEMS STRENGTHENING (RSS)

THE CASE FOR WHO’S PREQUALIFICATION

NORMS AND STANDARDS
Some of the global challenges that need to be addressed

### Functionality of National Regulatory Authority

<table>
<thead>
<tr>
<th>Year</th>
<th>Medicines and vaccine</th>
<th>Medical devices</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>50</td>
<td>33</td>
</tr>
<tr>
<td>2017</td>
<td>60</td>
<td>38</td>
</tr>
<tr>
<td>2019</td>
<td>72</td>
<td>48</td>
</tr>
<tr>
<td>2021</td>
<td>84</td>
<td>60</td>
</tr>
</tbody>
</table>

194 WHO Member States

- **50%** Developed
- **30%** Limited
- **20%** Variable

≈30% of NRAs globally have capacity to perform all core regulatory functions for medicines (much less for biotherapeutic products)
MOVING TOWARDS WHO-LISTED AUTHORITIES

‘Stringent Regulatory Authority’

- originally based on ICH membership
- developed to promote reliance and guide procurement decisions
- widely used and recognized

Growing recognition that change was needed

- interim definition endorsed by WHO ECSPP at 51st meeting
- new approaches agreed at the 52nd meeting
EXPERTS AT 52ND MEETING (OCT 2017) RECOMMENDED:

- Term SRA be replaced by *WHO-Listed Authority (WLA)*
- Currently identified “SRAs” will be regarded as WHO-Listed
- Use of WHO Global Benchmarking Tool + completion of confidence-building process - additional NRAs
- Procedure for listing to be developed through usual public consultation process
BENCHMARKING OF REGULATORY SYSTEMS

- **WHO**’s Global Benchmarking Tool (GBT) posted for public consultation January-February 2018
- Over **1100** comments received - Member States, industry associations and other stakeholders - fully supportive
- Comments under review - meeting of regulatory experts in July 2018
- Updated revision VI is expected to be published by **Oct/Nov 2018**
- Significant milestone for regulatory system strengthening efforts
  - A WHO HQ/PAHO collaboration
ROADMAP FOR PHASING IN GBT REVISION VI

- Pilot the GBT revision V
- Final adjustment, editing and publication of GBT revision VI in 2018
- Phasing in of GBT Revision VI in 2019
- GBT revision VI in Spanish and French in Q1
WHO GBT PERFORMANCE MATURITY LEVELS

1. NO FORMAL APPROACH
   Some elements of regulatory system exist
   Can be consider as functional if rely on other regulators for some specific functions
   99 COUNTRIES

2. REACTIVE APPROACH
   Evolving national regulatory system that partially performs essential regulatory functions
   45 COUNTRIES

3. STABLE FORMAL SYSTEM APPROACH
   Stable, well-functioning and integrated regulatory system
   Target of WHA Resolution 67.2
   50 COUNTRIES

4. CONTINUAL IMPROVEMENT EMPHASIZED
   Regulatory system operating at advanced level of performance and continuous improvement
   Advanced/reference Regulatory Authorities

ISO 9004
WHO GBT
COUNTRY EXAMPLE: UNITED REPUBLIC OF TANZANIA

- TFDA established in 2003 - collaboration with WHO
- WHO GBT in Nov 2016 - institutional development plan (IDP) to address gaps
- TFDA strictly implemented all the recommendations received as part of the IDP

Using the WHO Global Benchmarking Tool in May 2018:

- Benchmarked against 260 indicators to achieve ML 3 in 8 core functions
- Met 176 out of 190 critical indicators to reach ML 3
- All functions scored above 80% of implementation
- On target to achieve ML 3 as the first documented NRA in Africa before end of 2018 – a major milestone for Africa

08/10/2018
PREFORQUALIFICATION PROCESS

EXPRESSION OF INTEREST

PRODUCT DOSSIER SITE
MASTER FILE

ASSESSMENT

ACCEPTABLE

ADDITIONAL INFORMATION & DATA

PREQUALIFICATION

COMPLIANCE
Closing letter WHOPIR

CORRECTIVE ACTIONS
Follow-up (Notice of concern)

INSPECTIONS
FPP: GMP -API: GMP
CRO/BE: GCP/GLP

Variations
Requalification

MAINTENANCE & MONITORING
COLLABORATIVE REGISTRATION

Routine inspections - Special inspections - Handling complaints
PREQUALIFICATION - MEASURABLE IMPACT

- Median times shown as of Jun 2017, for dossiers accepted after 2012 for Rx & Vx, and after 2013 for Dx
- Between Feb 2013 and Dec 2017
THE COLLABORATIVE REGISTRATION PROCEDURE (CRP)

PRINCIPLES

- WHO PQ shares the reports that served as the basis for the prequalification decision, so that NRAs do not conduct assessment and inspections
- National registration based on PQT evaluation

DIAGNOSTICS
Procedure in development
Ongoing discussions with NRAs

MEDICINES
Started in 2012
As of February 2018:
- 35 countries + CARICOM
- 299 registrations for 77 medicines
- 85 days median local time for registration*

VACCINES
Procedure published in 2007, harmonized for medicines and vaccines as of 2014
In 2015:
- Adopted by expert committee (ECBS)
WHO PREQUALIFICATION: LOOKING FORWARD

- **Expand scope** to cover additional products on the EML:
  - set up criteria for prioritisation
  - SBP pilot, NCDs (Diabetes/Insulin, Hypertension)
  - IVDs for Cholera, TB, NCDs, NTDs/Dengue
- **Gradually expand the mechanisms** for PQ through:
  - Reliance on regional-network-joint-assessments
  - Expand the abridged assessment approaches
- **Expand risk based approaches** - ERP, ERPD, EUAL and other mechanisms for Snake anti-venoms, Rabies vaccine, RSV, DAT, etc..
PREQUALIFICATION PILOT - RITUXIMAB & TRASTUZUMAB

• Listed in the EML + WHO technical guidance for evaluation
• Some SRAs - extensive experience in evaluating these products
• Multiple Manufacturers– potential for competition – increased access

ASSESSMENT PATHWAYS

• Abridged assessment where approved by SRAs and marketed in the country of registration
• Full assessment of SBPs for rituximab or trastuzumab that have been registered by non-SRAs and marketed in the country of registration
• Commitment to pursue collaborative registration in participating countries – reliance
WHO NORMS AND STANDARDS

Technical report series

85 MEDICINES QUALITY ASSURANCE GUIDELINES

93 VACCINES AND BIOThERAPEUTIC PRODUCTS GUIDELINES OR RECOMMENDATIONS

International Pharmacopoeia

+ 540 SPECIFICATIONS
GUIDELINES

BIOTHERAPEUTIC PRODUCTS
Procedures and data requirements for changes to approved biotherapeutic products

IN VITRO DIAGNOSTICS
• HIV rapid diagnostic tests for professional use and/or self-testing
• Establishing stability of in-vitro diagnostic medical devices

VACCINES
Quality, safety and efficacy of Ebola vaccines
HERBAL MEDICINES
• Good herbal processing practices
• Good manufacturing practices

WHO GUIDANCE ON TESTING OF “SUSPECT” FALSIFIED MEDICINES

GOOD PHARMACOPOEIAL PRACTICES
• Chapter on monographs on herbal medicines
• Chapter on monographs for compounded preparations

HEATING, VENTILATION AND AIR-CONDITIONING SYSTEMS FOR NON-STERILE PHARMACEUTICAL PRODUCTS …
Safety monitoring of medicines and health products is essential to protect people from harm

• New products in LMICs developed in well-resourced settings - baseline safety data may not be entirely applicable to the resource constrained settings

Smart Safety Surveillance – risk-based prioritization for PV

• To strengthen pharmacovigilance capacity in LMICs
• Establish end-to end safety surveillance of products from their clinical development to the post-market stages
• Pilot ongoing in 2 countries with selected medicines and vaccines

CONSTRAINED ACCESS TO MEDICINE

Availability
Affordability
Acceptability

WEAK TECHNICAL CAPACITY
Poor oversight
Lack of resources
Limited awareness

POOR GOVERNANCE PRACTICES
Poor procurement
Unethical practice
Corruption
WHO GLOBAL SURVEILLANCE SYSTEM

Available in English, French, Spanish and Portuguese

150 member States trained
700 regulatory personnel trained
18 large procurement agencies sensitized
1600 Suspect Products Reported

106 Countries where incidents occurred
24 WHO Global Drug alerts and numerous warnings
22 Workshops in all regions

WHO Technical Assistance in over 100 cases
RECENT WHO REPORTS (NOVEMBER 2017)

http://www.who.int/medicines/regulation/ssffc/publications/se-study-sf/en
Observed failure rate of analysed medical product samples from low and middle-income countries: 10.5%

Estimated spending on SF medical products in low and middle-income countries based on unweighted estimates of pharmaceutical sales: US$ 30.5 BILLION
Impact Model Findings:

72,430 – 169,271 estimated DEATHS caused by SF antibiotics used by children under 5 with childhood pneumonia*

31,000 – 116,000 estimated DEATHS caused by SF products used by patients suffering from malaria in sub-Saharan Africa**

US$ 38.5 million Estimated spending on SF anti-malarials in sub-Saharan Africa

* University of Edinburgh
** London School of Hygiene and Tropical Medicine
DEMOCRATIC REPUBLIC OF CONGO

- Remote rural area
- Low literacy levels
- Poor access to medicines
- Civil unrest
Containers labelled Diazepam containing an overdose of anti-psychotic medicine - Haloperidol

- Irrational use of Diazepam
- Limited Access in the region
- Illegal cross border supply
- Unethical / Criminal practice by distributors
- Little regulatory oversight

FALSIFIED MEDICAL PRODUCTS

3 medical centres
100 medical staff
1000 hospitalizations
11 deaths
Coartem – Anti malarial
1,383,528 packs

Postinor 2 – Emergency Contraceptive
4,930 packs

Vermox – Worming treatment
1,534 packs

Clomid – Fertility treatment
36,550 packs

Clamoxyl - Antibiotic
744 packs
AFRICAN CUSTOMS SEIZURE ANGOLA

WHO GSMS data; 2013-2017

- Antiinfectives
- Antiparasitics
- Nervous system
- Alimentary tract and metabolism
- Genito-urinary
- Antineoplastic and immunomodulators
- Musculo-skeletal system
- Cardiovascular system
- Various
- Respiratory system
- Blood and blood forming organs
- Systemic hormonal preparations
- Dermatologicals
- Sensory organs

[Graph showing the distribution of seized goods by WHO GSMS data for 2013-2017]
Political will is required to translate policy agreed at the global level to sustainable actions on the ground with appropriate financial and human resources.

Strengthening regulatory capacity and systems is a key step and good investment to safeguard the manufacture, distribution and supply of medical products.

Improved reporting systems and greater transparency within and between countries is required, together with wide and effective multi stakeholder engagement.
“No family should endure financial hardship for out-of-pocket payments for the purchase of medicines to treat their loved ones, and no man, woman or child should die simply because they cannot access the life-saving medicines they need.”

Dr Tedros Aghanom Ghebreyesus