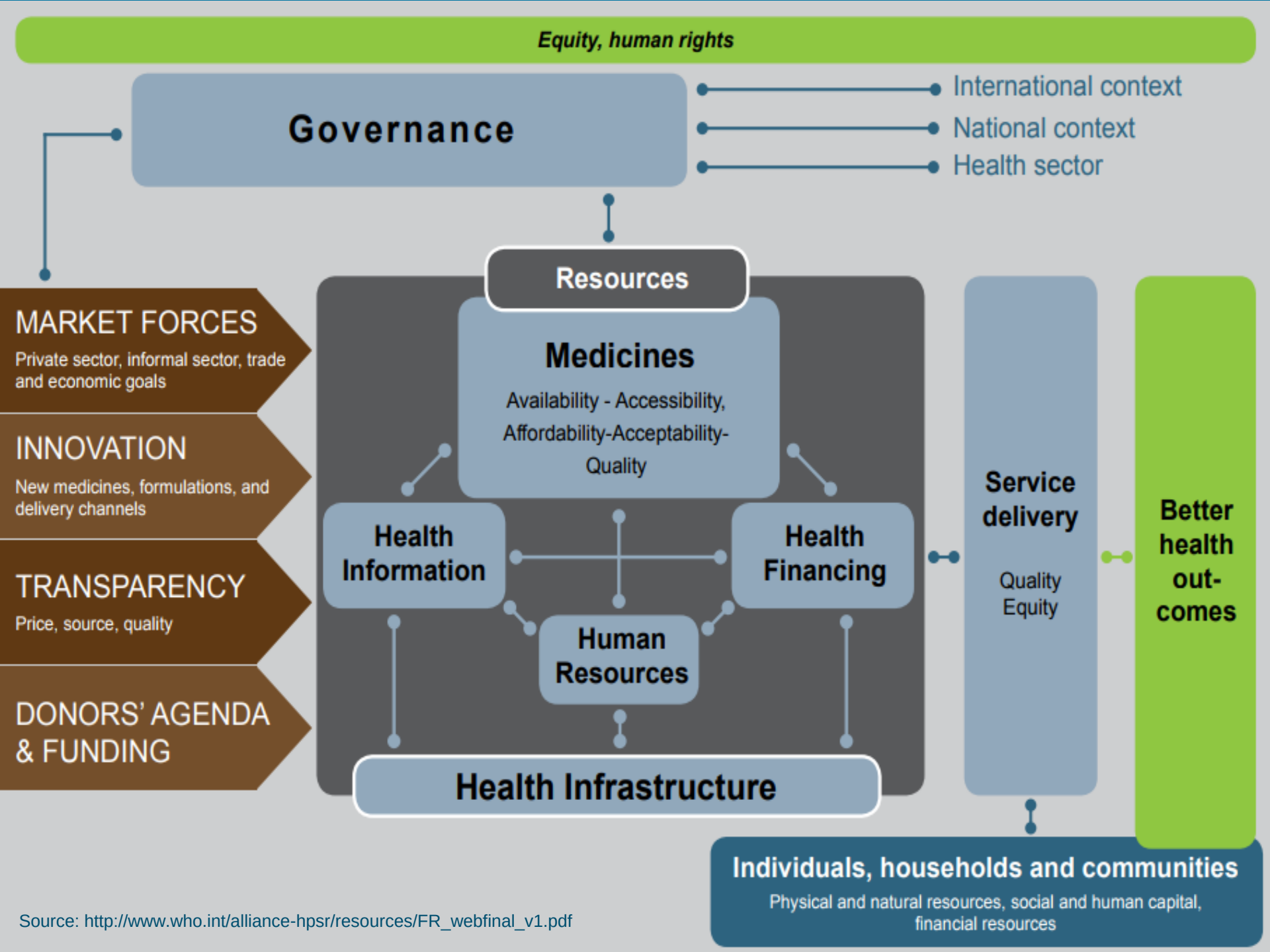
World Health Organization

WIPO Standing Committee of the Law of Patents

Sharing Session on “Patents and Health”

12 December 2017

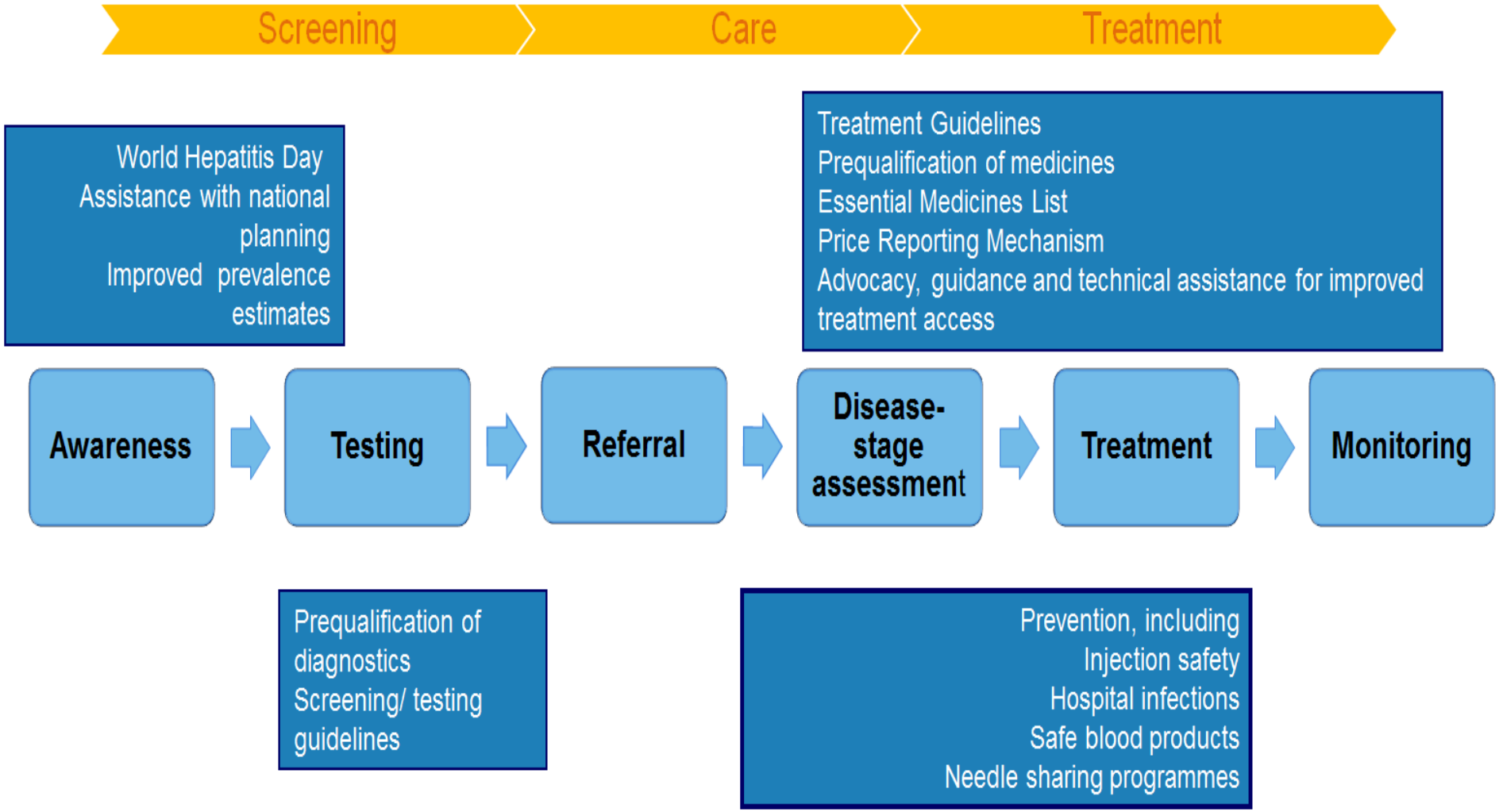
Peter Beyer | Senior Advisor | Essential Medicines & Health Products | Switzerland



Source: http://www.who.int/alliance-hpsr/resources/FR_webfinal_v1.pdf

WHO's Role in Fighting Hepatitis

World Health Organization



World Health Organization

Prevention strategies for hepatitis B & C

- Hepatitis B vaccination (mother, child, healthcare workers)
- Safe blood products
- Safe injection practices
- Standard and transmission-based precautions
- Harm reduction services for people who inject drugs
- Promotion of safe sex

Sources: http://www.who.int/injection_safety/en/
http://www.who.int/patientsafety/en/

"Access" is more than "making medicines available."

Equitable Access to Medicines

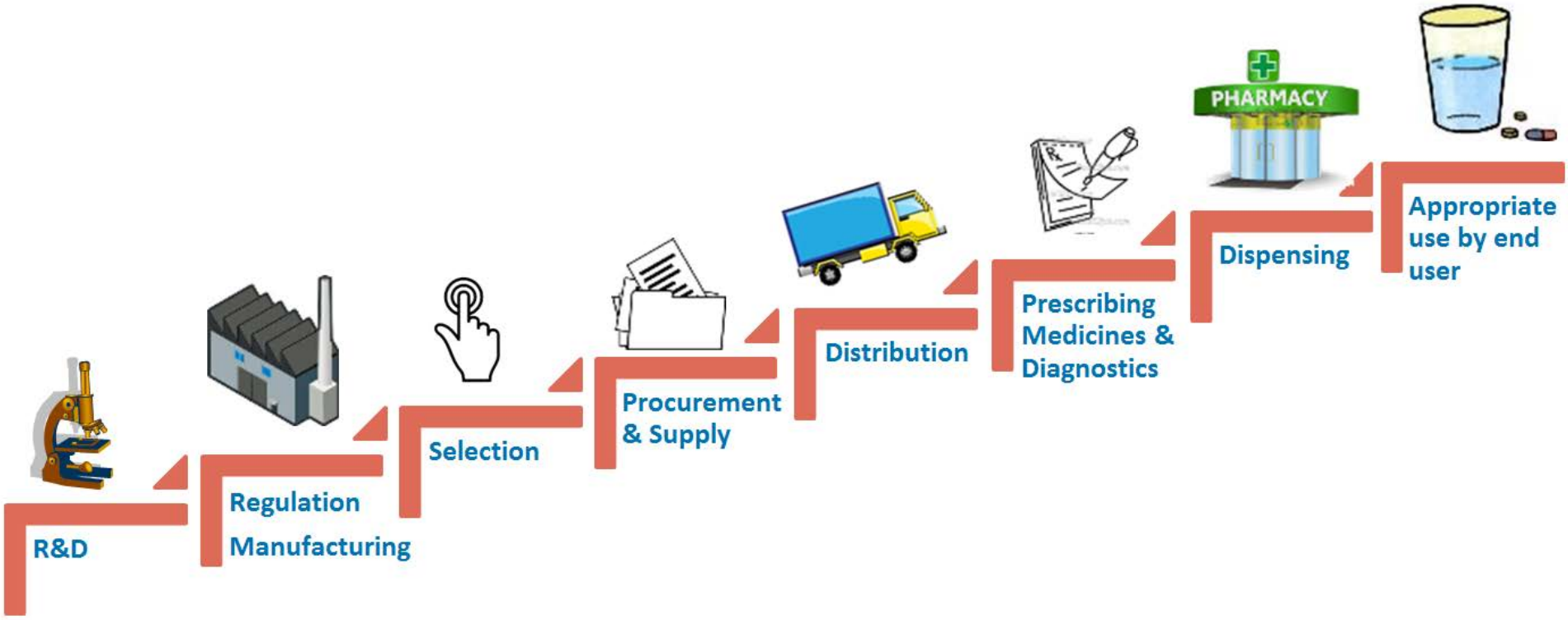
To provide "access," countries need to provide:

- the right products…
  - in the right places,
  - at the right time,
  - at the right price, and
  - to ALL people who need them.

WHO Framework for Access to Medicines

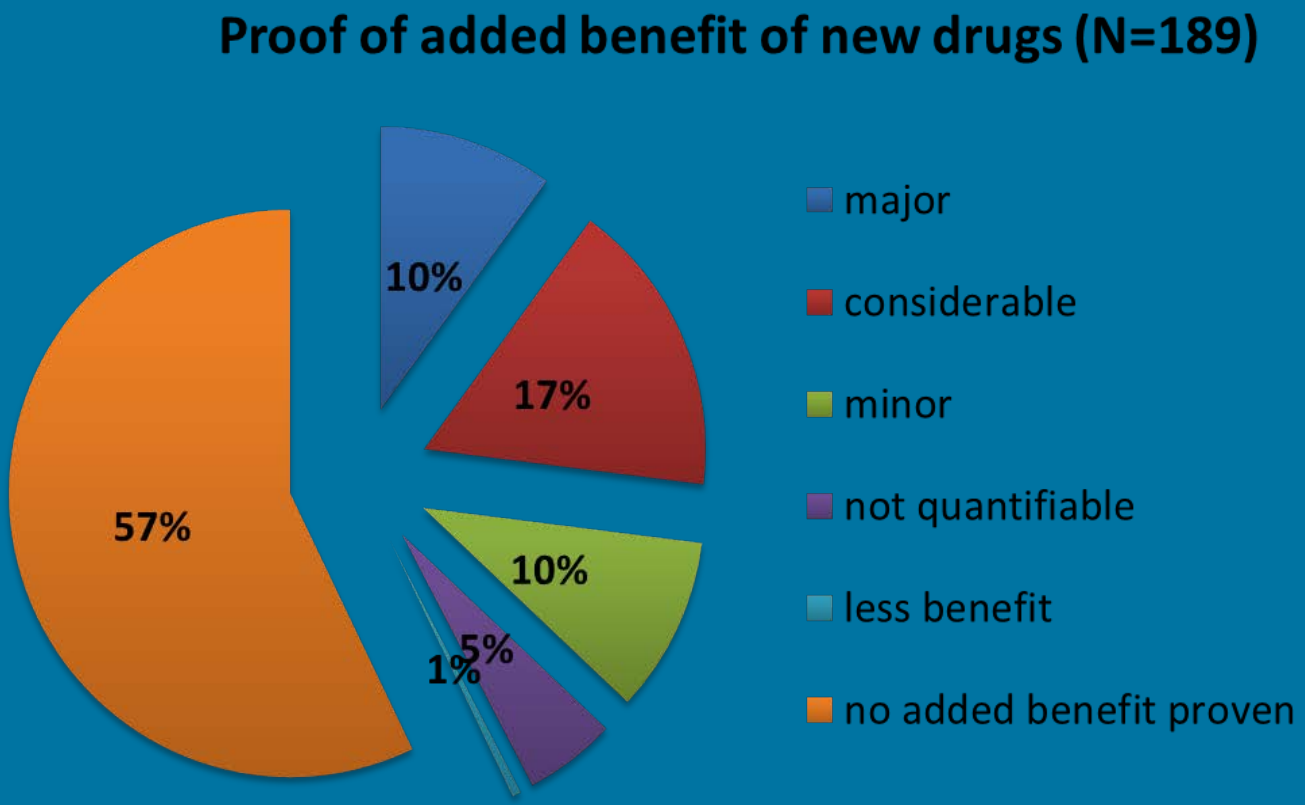
World Health Organization

Covers the whole value chain



Source: http://www.who.int/phi/promoting_access_medical_innovation/en/

Does New Mean Better?

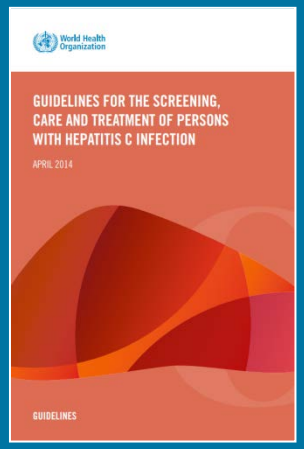


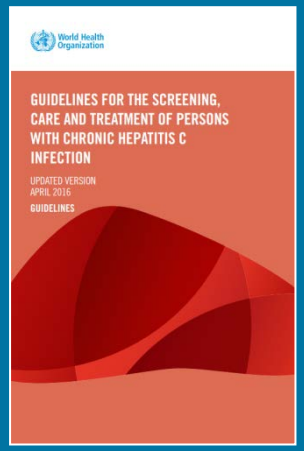
Source: Access to medicines in the Baltics: changing the narrative – courtesy by Beate Wieseler, IQWiG

World Health Organization

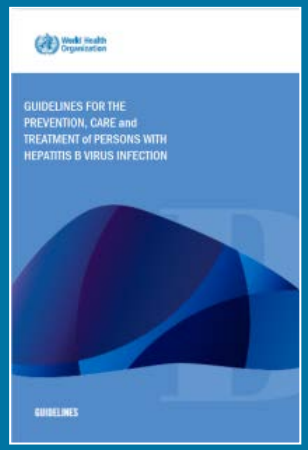
WHO Hepatitis Normative Guidance

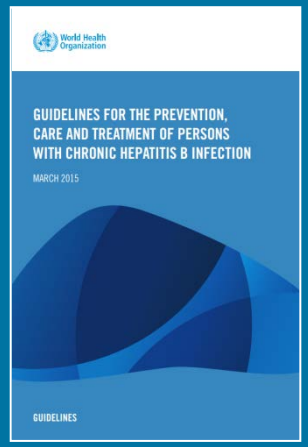
HCV (2014+2016)



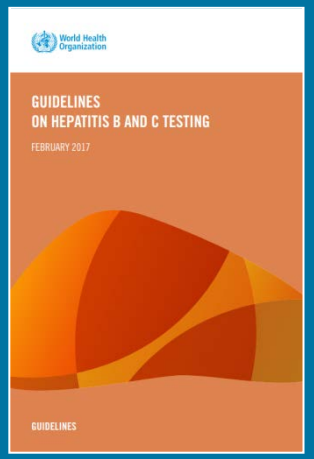


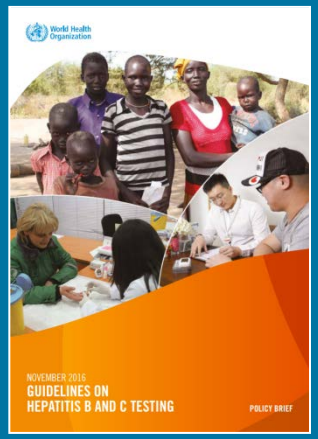
HBV (2015)





Testing (2017)





WHO Essential Medicines List(s)

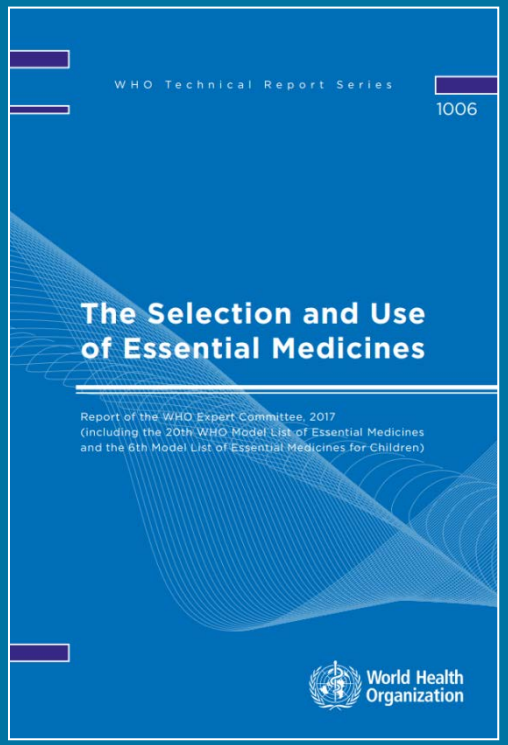
Satisfy priority health care needs, should be available at all times in appropriate dosage forms, of assured quality at affordable price

Contains 433 medicines (20th EML) deemed essential

Revised every two years

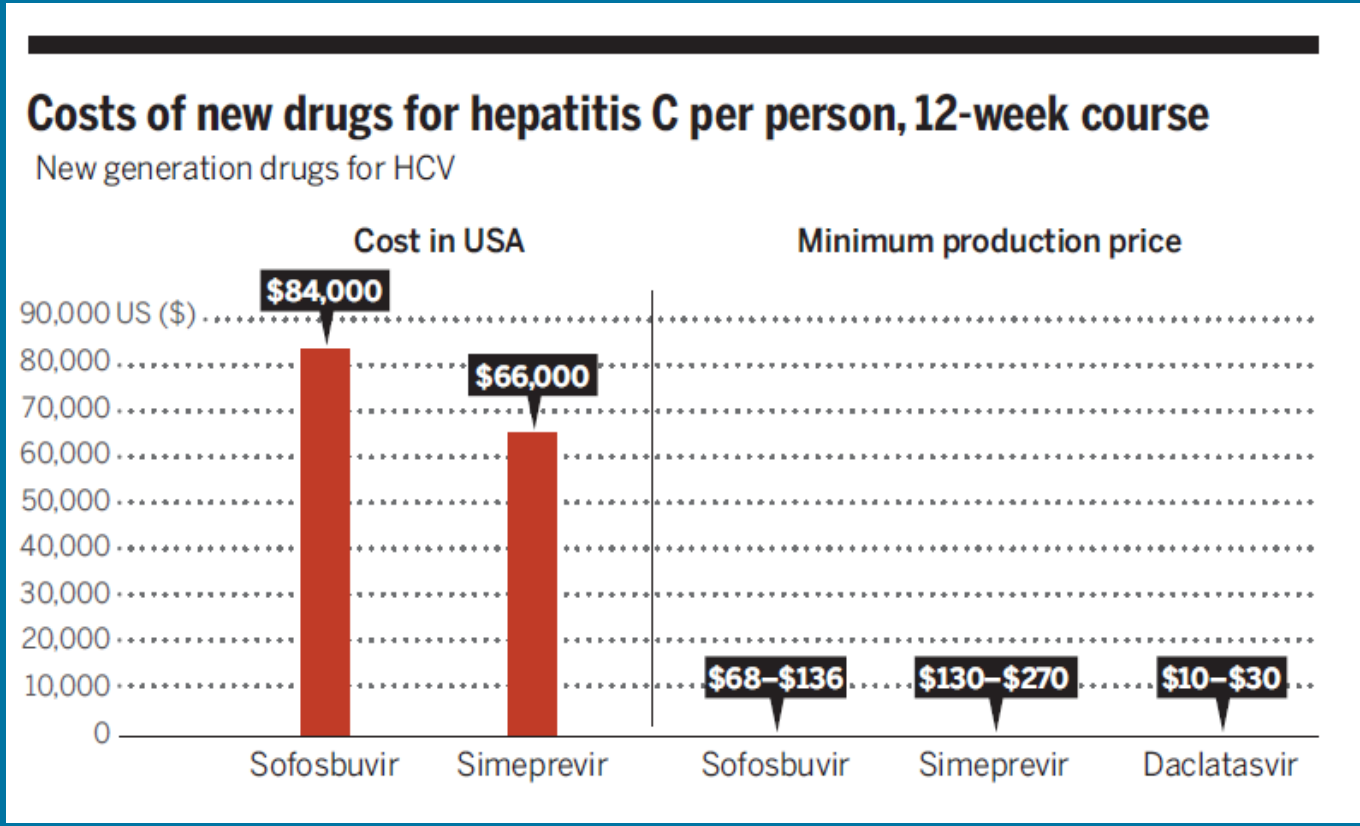
Updated in June 2017

- Added 30 medicines for adults, 25 for children
- Specifies new uses for 9 already-listed products
- Provides new advice on which antibiotics to use for common infections and which to preserve for the most serious syndromes
- New patented DAAs for treatment of HepC added in 2015 and 2017 revisions



Price vs Production Costs

World Health Organization



Source: Hill A, Cooke G. Science 2014: Vol. 345 no. 6193 pp. 141-142

Le Matin

SANTÉ L'INDE AU SECOURS DE LA SUISSE CONTRE L'HÉPATITE C

Le traitement normal est tellement onéreux qu'il est limité à certains patients. Une caisse d'assurances a décidé de se fournir en Inde, pour nettement moins cher.

Different Determinants of Price

- Competition is the most important factor with intellectual property being an important determinant for competition
- Companies' pricing policies, including differential pricing
- Costs and mark ups in the supply chain
- Taxes and tariffs
- Government pricing and reimbursement policies
- …

Intellectual Property Impacting Generic Entry

- Regular patent protection
- Patent term extensions
- Secondary patents, e.g. combination patents, patents on variations of chemical molecules
- Data exclusivity, example of Ukraine
- Other forms of market/data exclusivity
- Practices such as “pay-for-delay”

WHO Patent Landscapes

World Health Organization

sofosbuvir (updated)	Harvoni	Gilead Sciences
ledipasvir (updated)		Gilead Sciences
Daclatasvir (updated)		BMS
dasabuvir	Viekira Pak with ritonavir	AbbVie
ombitasvir		AbbVie
paritaprevir		AbbVie
simeprevir		Janssen

Source: www.who.int/phi/implementation/ip_trade/ip_patent_landscapes/en/

Sofosbuvir: Expiry without patent term extension(s)

Market Authorization US: 2013/14

2024
- Broad compound patent (Markush)
- WO2005003147A2

2028
- Compound patent on prodrug
- WO2008121634A2

2031
- Crystalline forms
- WO2011123645A2

2032
- Combination with ledipasvir
- WO2013040492A

2032
- Composition & dosage
- WO2013082003A1

Source: www.who.int/phi/implementation/ip_trade/ip_patent_landscapes/en/

PATENT LANDSCAPE IMATINIB	Patent 1	Patent 2	Patent 3
	Pyrimidine Derivatives & their Preparation Covers base compound imatinib, pharma-ceutically acceptable salt, method of use for chemotherapy, […]	**Crystal Modification of a N-Phenyl-2-Pyrimidineamine […]** Covers the beta crystalline form of imatinib (imatinib mesylate)	**Treatment of Gastrointestinal Stromal Tumors** Covers use of imatinib mesylate for treatment of gastrointestinal stromal tumors – GIST
Patent No.	US 5,521,184	EP 0998473 B1	WO2002/34727
Expected Expiry	**25 March 2013**	**16 July 2018**	**26 October 2021**
Brazil	Granted Patent No. PP1100739 (expired)	App No. PI9810920 Refused – Under Appeal	App No. PI0114870 Refused – Under Appeal
China	Granted Patent No. 1043531 (expired)	Granted Patent No. 1134430	Granted Patent No. 1276754
European Patent Office (EPO)	Granted Patent No. 0564409 (expired)	Granted Patent No. 0998473	Granted Patent No. 1332137
India	Not filed	App 1602/MAS/1998 Refused following pre-grant oppositions	No patent
Kenya (ARIPO)	Not filed	Not filed	Not filed
OAPI	Not filed	Not filed	Not filed
South Africa	Granted Patent No. 9302397 (expired)	Granted Patent No. 9806362	Granted Patent No. 200302155

Source: http://www.who.int/phi/publications/int_prop_local_prod_opportunities_chanllenges/en

Overcoming Patent-related Barriers to Access

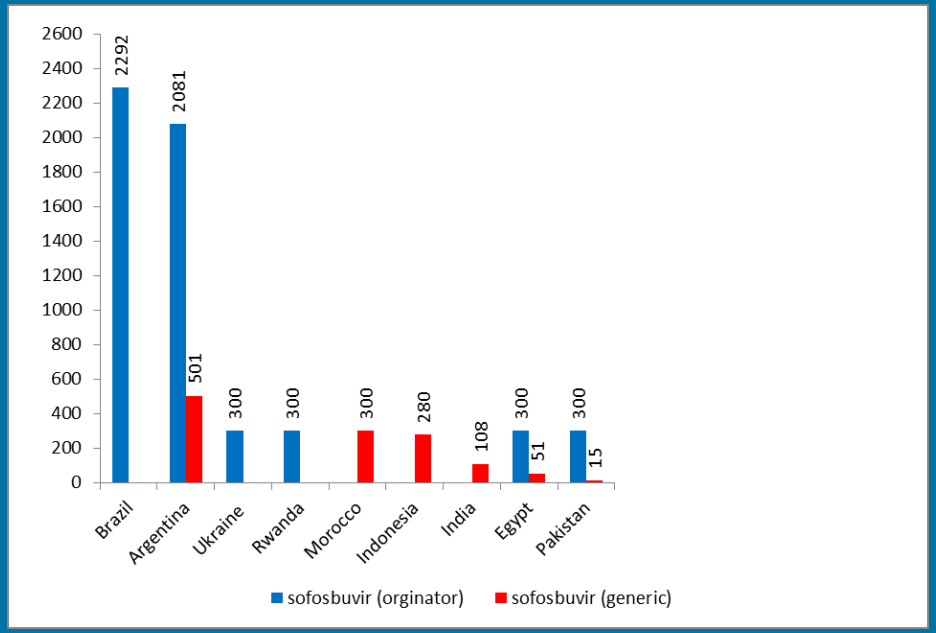
World Health Organization

- Voluntary licenses
  - daclatasvir 112 countries > 2/3 thirds of middle-income countries / 68.6% of disease burden LMICs (MPP)
  - sofosbuvir, sofosbuvir/ledipasvir, and sofosbuvir/velpatasvir : 105 countries - 31 LICs, 2 HICs (Equatorial Guinea & Seychelles), 72 MICs
- Local production where there are no patents
  - e.g. Argentina, Bangladesh, India, Egypt, Morocco, Pakistan
- Patent oppositions/strict patentability criteria
- Compulsory licensing/government use, e.g. Malaysia

Prices of Hepatitis C drugs are dropping (where there are generics)

World Health Organization

- In Egypt, the price for a 3-month Hepatitis C treatment dropped from US$ 900 in 2014 to less than US$ 200 in 2016
- Prices of Hepatitis C drugs continue to vary considerably across countries
- The steepest price decrease is observed in countries with generic competition, confirming experience with HIV treatment



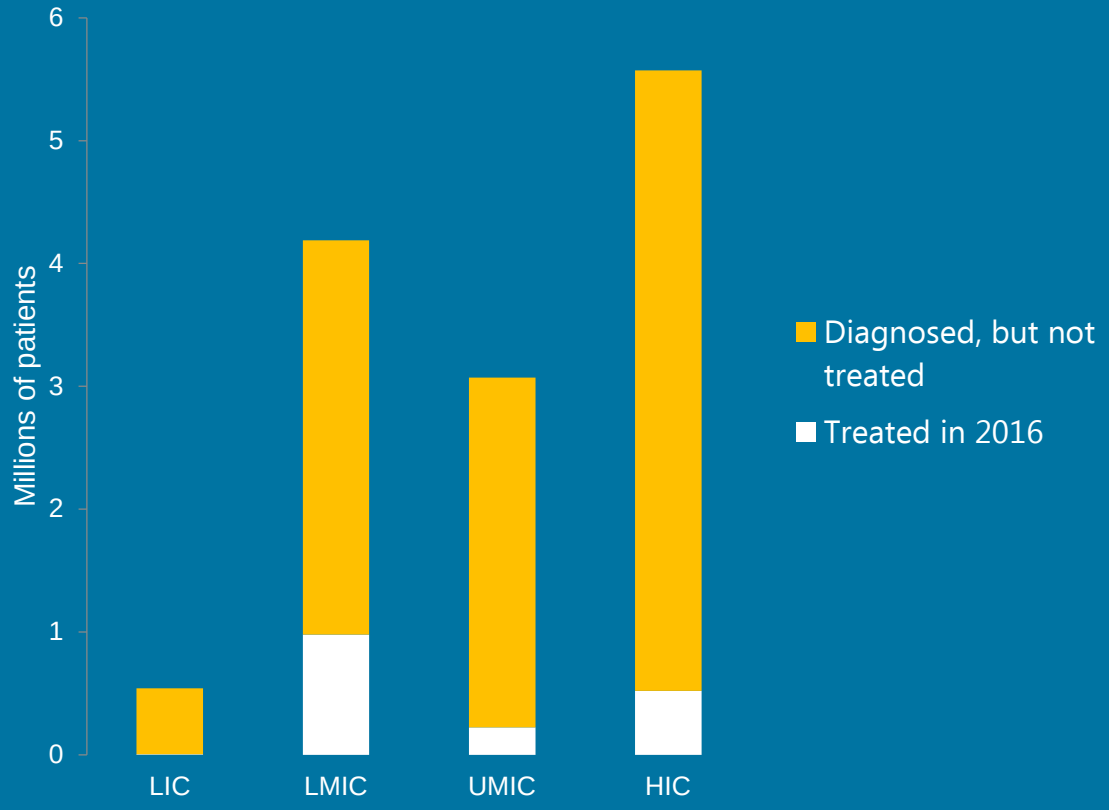
Prices of sofosbuvir per bottle (US$)
innovator (blue), generic (red)

Data from
WHO survey 2016

HCV Treatment Coverage with DAAs is Heterogeneous

World Health Organization

Onset of DAA treatment among the 13 million diagnosed with HCV infection, by income group, 2016



- In 2017, 62% of HCV infected persons lived in countries that can procure generic DAAs (LIC, LMIC)
- In UMIC, the situation remains heterogeneous
- Egypt and Pakistan account for the largest numbers started on treatment in LMIC

Source: WHO on the basis of Center for Disease Analysis/Polaris

Procurement of Generic HBV Medicines

Public sector procurement with high volumes can lead to competition and low prices

Most persons with HBV infection live in LIC and MIC, that can procure generic medicines

- Quality generic medicines are available for procurement
  - Tenofovir < USD 30 /year
  - Entecavir ~ USD 400 /year
- However, few countries have a hepatitis programme
- Fragmented procurement leads to high prices

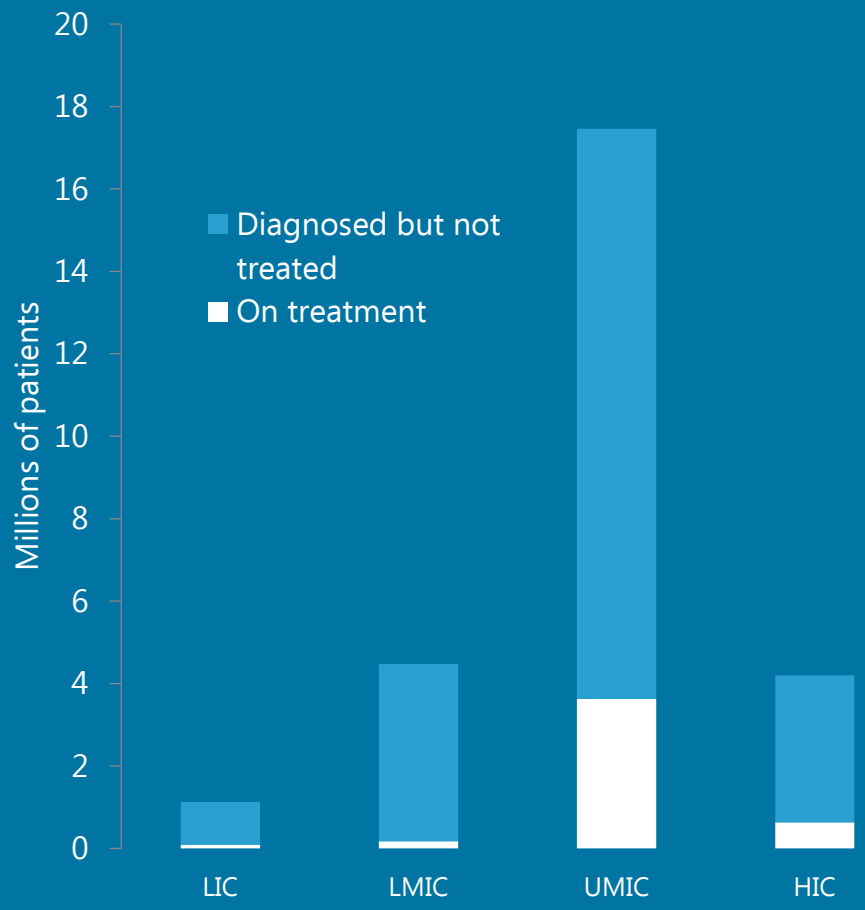
Other countries will be able to buy affordable generics in 2018 as the tenofovir patents are due to expire

- Most high income countries
- China and Mexico

HIC: High income countries
UMIC: Upper middle income countries
LMIC: Lower middle income countries
LIC: Low income countries

HBV Treatment Coverage Remains Low

Treatment coverage among the 27 million diagnosed with HBV, by income group, 2016



- China accounts for most new treatments
- Generic tenofovir is mostly accessed as a fixed dose combination for HIV treatment
- There is little procurement of generic tenofovir and entecavir for monoinfected patients

Source: WHO on the basis of Center for Disease Analysis/Polaris

Accelerating DAA Registration Status

- In many countries, new DAAs are still not registered and consequently not available
- Some countries require additional local trials
- Importance of the registration of the originator company products – FDCs and single component – to enable generic registration
- WHO pre-qualification speeds up registration process and introduction of generics
- Strong role of advocacy

Procurement

Effective & Efficient Procurement Systems

- Procurement systems should be designed to obtain selected medicines and other medical products of good quality, at the right time, in the required quantities, and at favorable costs.

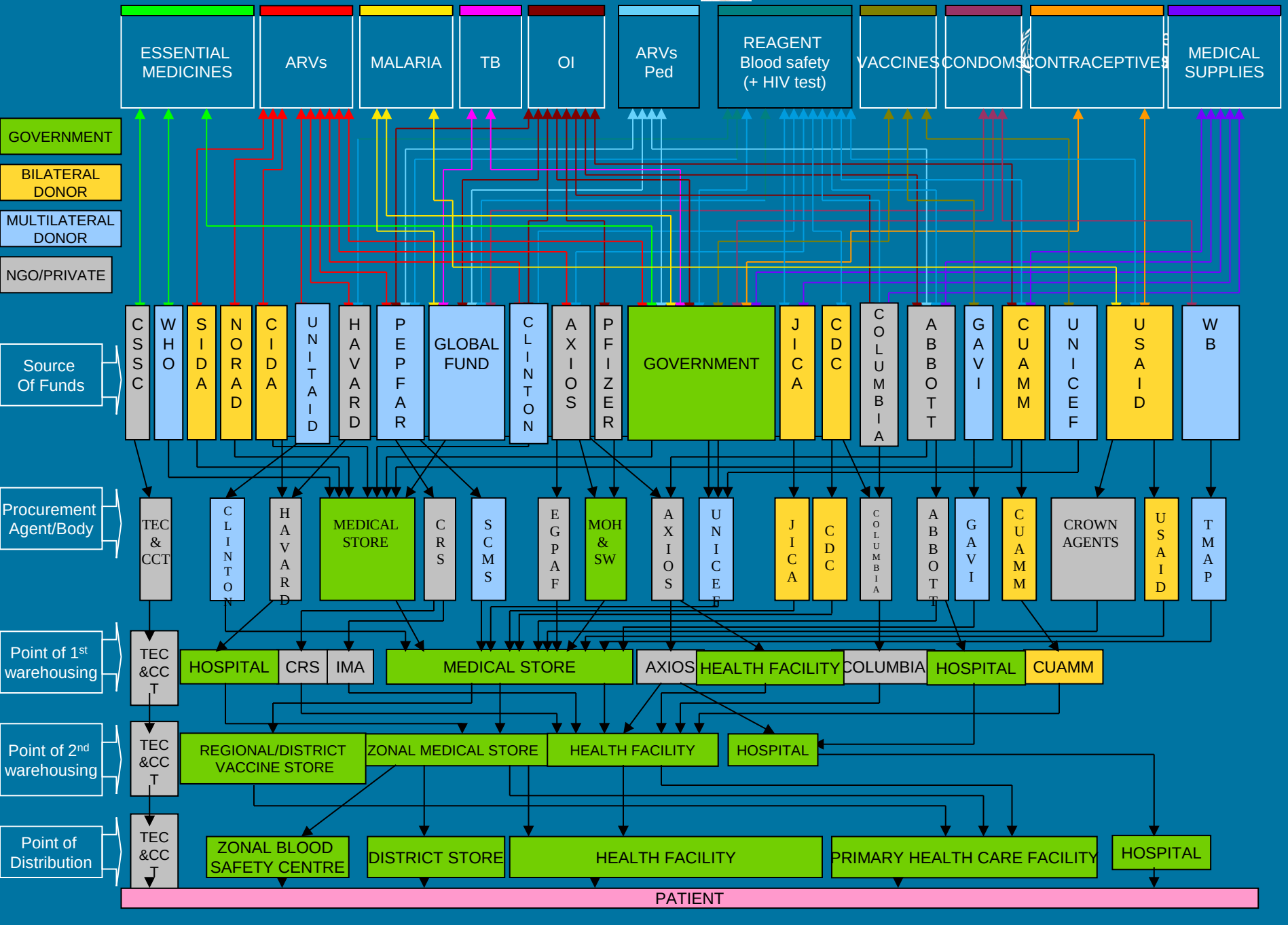
Principles for effective procurement

- Divide different procurement functions and responsibilities (selection, quantification, product specification, pre-selection of suppliers and adjudication of tenders) among multiple parties and give each one of them the necessary expertise and resources to do their particular job.
- Ensure transparency of procurement and tender procedures, follow written procedures throughout, and use explicit criteria to award contracts.
- Provide for a reliable management information system that functions to plan, and monitor procurement on a regular basis, including through the execution of an annual external audit.
- Limit public-sector procurement to an essential drugs list or national/local formulary list so as to ensure that the necessary products are procured.
- List drugs by their INN/generic name, on procurement and tender documents.
- Quantify procurement orders based on past consumption, provided that such data have been proven to be accurate. Consumption data must be updated continually, in order to take into account changes in morbidity, and factors such as seasonality and prescribing patterns.
- Finance procurement using reliable mechanisms, such as decentralized drug purchasing accounts or revolving drug funds. In each case, the mechanism itself must also be adequately funded.
- Purchase the largest appropriate quantity in order to achieve economies of scale.
- Obtain favourable prices without compromising quality when procuring for the public sector.
- Monitor this process of procurement where prices are negotiated centrally but ordering done by individual health facilities in the periphery.
- Pre-qualification of possible suppliers is essential, and criteria such as product quality, reliability of service, time for delivery and financial sustainability should be considered.
- Assured quality of purchased medicines, according to international standards.

Source: http://www.who.int/phi/promoting_access_medical_innovation/en/

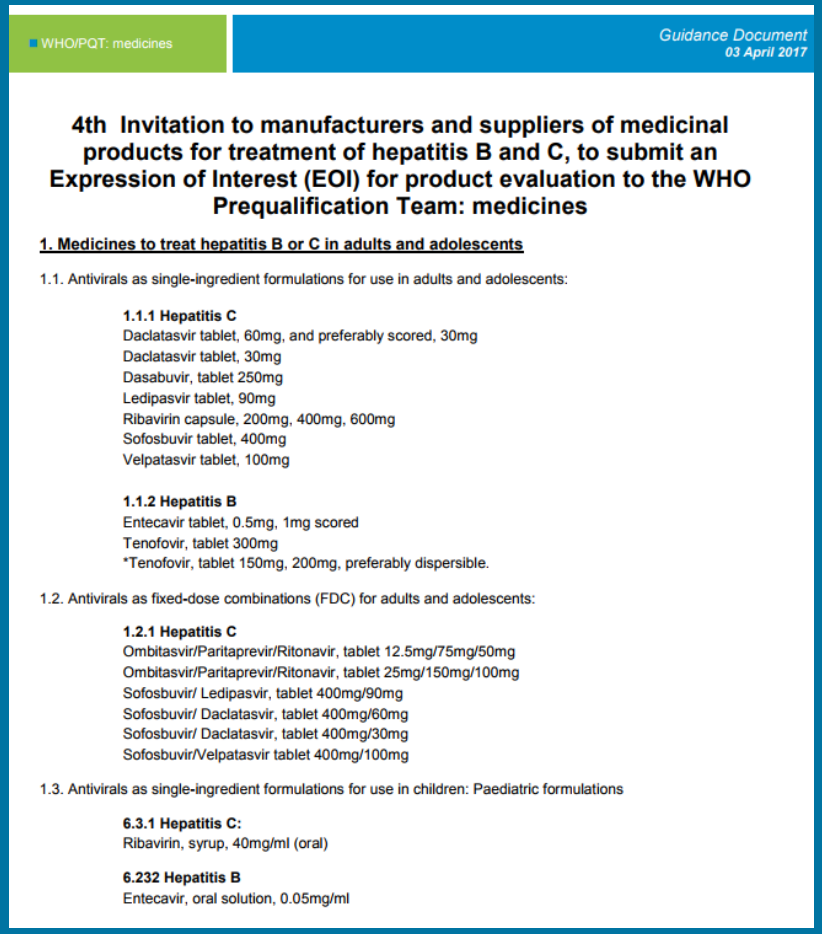
Medicines supply systems in TANZANIA. 2007

United Republic of Tanzania



UN/WHO Prequalification

Vision: Good quality medicines for everyone



WHO/PQT: medicines

Guidance Document
03 April 2017

4th Invitation to manufacturers and suppliers of medicinal products for treatment of hepatitis B and C, to submit an Expression of Interest (EOI) for product evaluation to the WHO Prequalification Team: medicines

1. Medicines to treat hepatitis B or C in adults and adolescents

1.1. Antivirals as single-ingredient formulations for use in adults and adolescents:

1.1.1 Hepatitis C
Daclatasvir tablet, 60mg, and preferably scored, 30mg
Daclatasvir tablet, 30mg
Dasabuvir, tablet 250mg
Ledipasvir tablet, 90mg
Ribavirin capsule, 200mg, 400mg, 600mg
Sofosbuvir tablet, 400mg
Velpatasvir tablet, 100mg

1.1.2 Hepatitis B
Entecavir tablet, 0.5mg, 1mg scored
Tenofovir, tablet 300mg
*Tenofovir, tablet 150mg, 200mg, preferably dispersible.

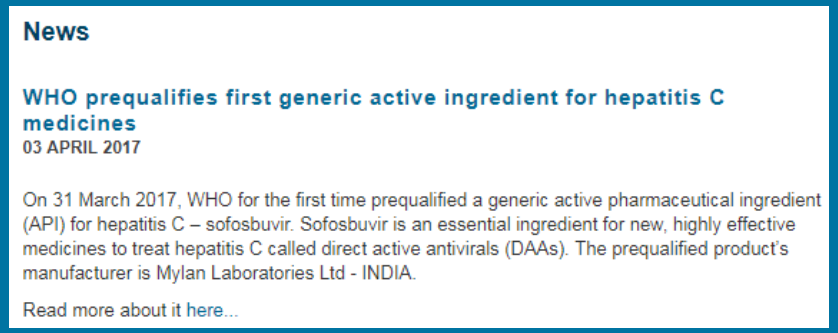
1.2. Antivirals as fixed-dose combinations (FDC) for adults and adolescents:

1.2.1 Hepatitis C
Ombitasvir/Paritaprevir/Ritonavir, tablet 12.5mg/75mg/50mg
Ombitasvir/Paritaprevir/Ritonavir, tablet 25mg/150mg/100mg
Sofosbuvir/ Ledipasvir, tablet 400mg/90mg
Sofosbuvir/ Daclatasvir, tablet 400mg/60mg
Sofosbuvir/ Daclatasvir, tablet 400mg/30mg
Sofosbuvir/Velpatasvir tablet 400mg/100mg

1.3. Antivirals as single-ingredient formulations for use in children: Paediatric formulations

6.3.1 Hepatitis C:
Ribavirin, syrup, 40mg/ml (oral)

6.232 Hepatitis B
Entecavir, oral solution, 0.05mg/ml



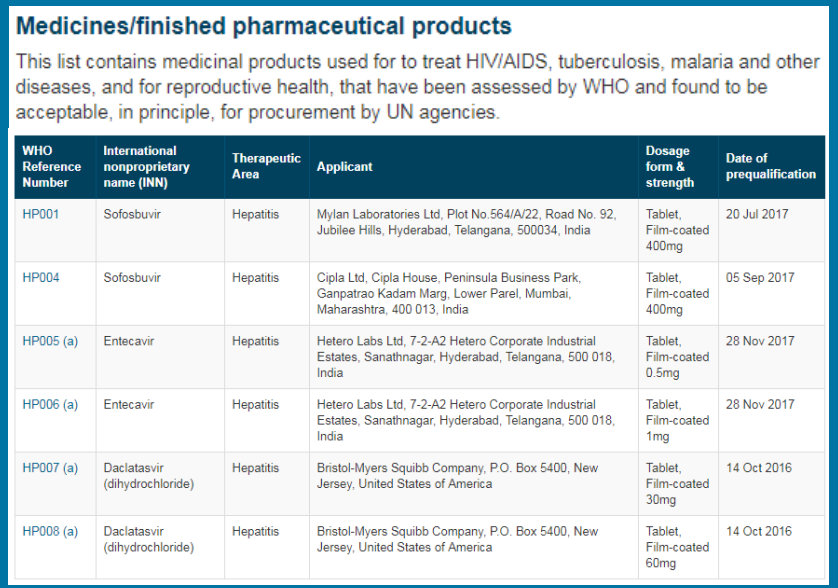
News

WHO prequalifies first generic active ingredient for hepatitis C medicines

03 APRIL 2017

On 31 March 2017, WHO for the first time prequalified a generic active pharmaceutical ingredient (API) for hepatitis C – sofosbuvir. Sofosbuvir is an essential ingredient for new, highly effective medicines to treat hepatitis C called direct active antivirals (DAAs). The prequalified product's manufacturer is Mylan Laboratories Ltd - INDIA.

Read more about it here...



Medicines/finished pharmaceutical products

This list contains medicinal products used for to treat HIV/AIDS, tuberculosis, malaria and other diseases, and for reproductive health, that have been assessed by WHO and found to be acceptable, in principle, for procurement by UN agencies.

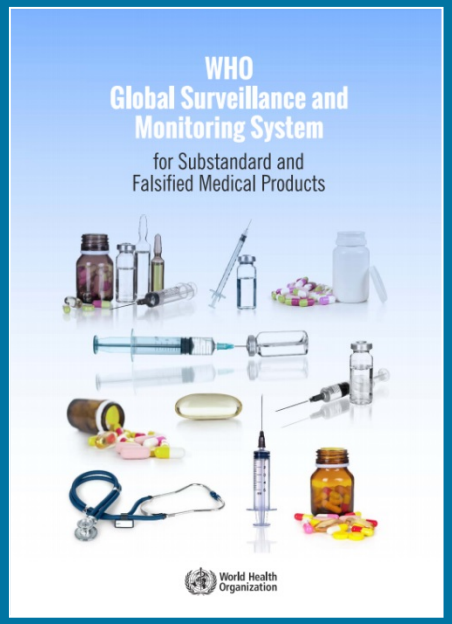
WHO Reference Number	International nonproprietary name (INN)	Therapeutic Area	Applicant	Dosage form & strength	Date of prequalification
HP001	Sofosbuvir	Hepatitis	Mylan Laboratories Ltd, Plot No.564/A/22, Road No. 92, Jubilee Hills, Hyderabad, Telangana, 500034, India	Tablet, Film-coated 400mg	20 Jul 2017
HP004	Sofosbuvir	Hepatitis	Cipla Ltd, Cipla House, Peninsula Business Park, Ganpatrao Kadam Marg, Lower Parel, Mumbai, Maharashtra, 400 013, India	Tablet, Film-coated 400mg	05 Sep 2017
HP005 (a)	Entecavir	Hepatitis	Hetero Labs Ltd, 7-2-A2 Hetero Corporate Industrial Estates, Sanathnagar, Hyderabad, Telangana, 500 018, India	Tablet, Film-coated 0.5mg	28 Nov 2017
HP006 (a)	Entecavir	Hepatitis	Hetero Labs Ltd, 7-2-A2 Hetero Corporate Industrial Estates, Sanathnagar, Hyderabad, Telangana, 500 018, India	Tablet, Film-coated 1mg	28 Nov 2017
HP007 (a)	Daclatasvir (dihydrochloride)	Hepatitis	Bristol-Myers Squibb Company, P.O. Box 5400, New Jersey, United States of America	Tablet, Film-coated 30mg	14 Oct 2016
HP008 (a)	Daclatasvir (dihydrochloride)	Hepatitis	Bristol-Myers Squibb Company, P.O. Box 5400, New Jersey, United States of America	Tablet, Film-coated 60mg	14 Oct 2016

Source: http://apps.who.int/prequal/
https://extranet.who.int/prequal/sites/default/files/documents/142_EOI%20hep%20B%26C_April2017_0.pdf

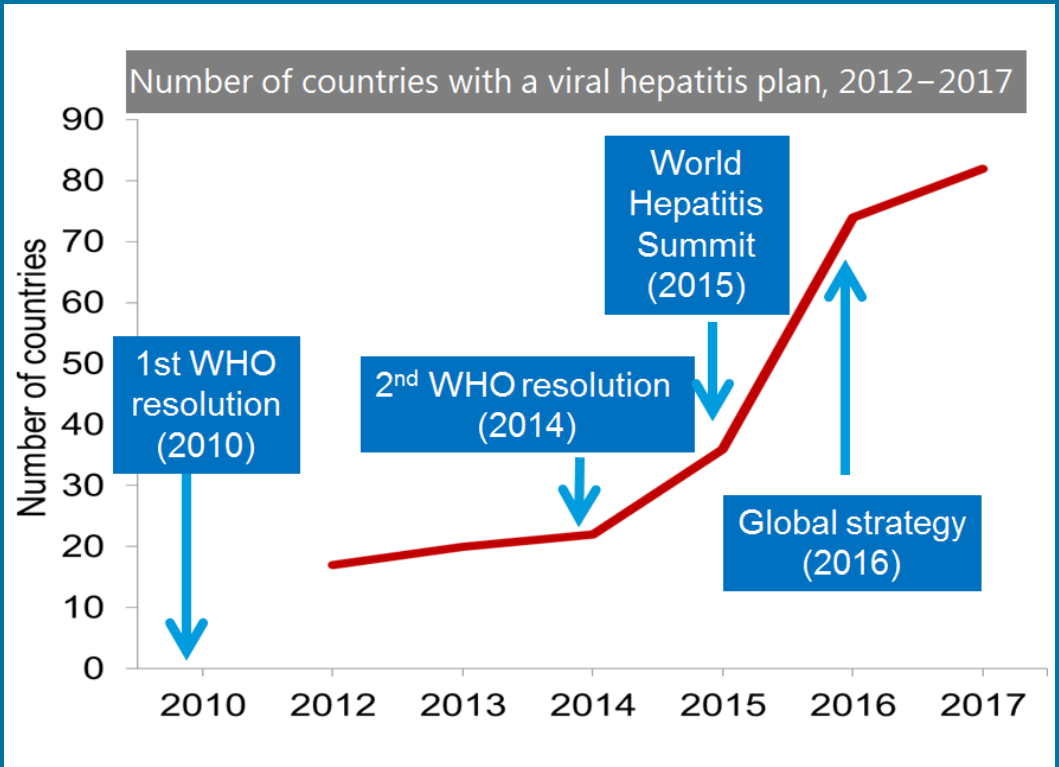
Substandard Falsified Medical Products

World Health Organization

- Reported to WHO from all main therapeutic categories, including medicines, vaccines and in vitro diagnostics
- Estimated 1 in 10 medical products in LMICs is substandard or falsified
- Most likely to reach patients in situations where there is constrained access to quality and safe medical products, poor governance and weak technical capacity
- WHO Surveillance and Monitoring System encourages countries to report incidents of substandard and falsified medical products in a structured and systematic format to help develop a more accurate and validated assessment of the problem



82 countries now have a viral hepatitis plan

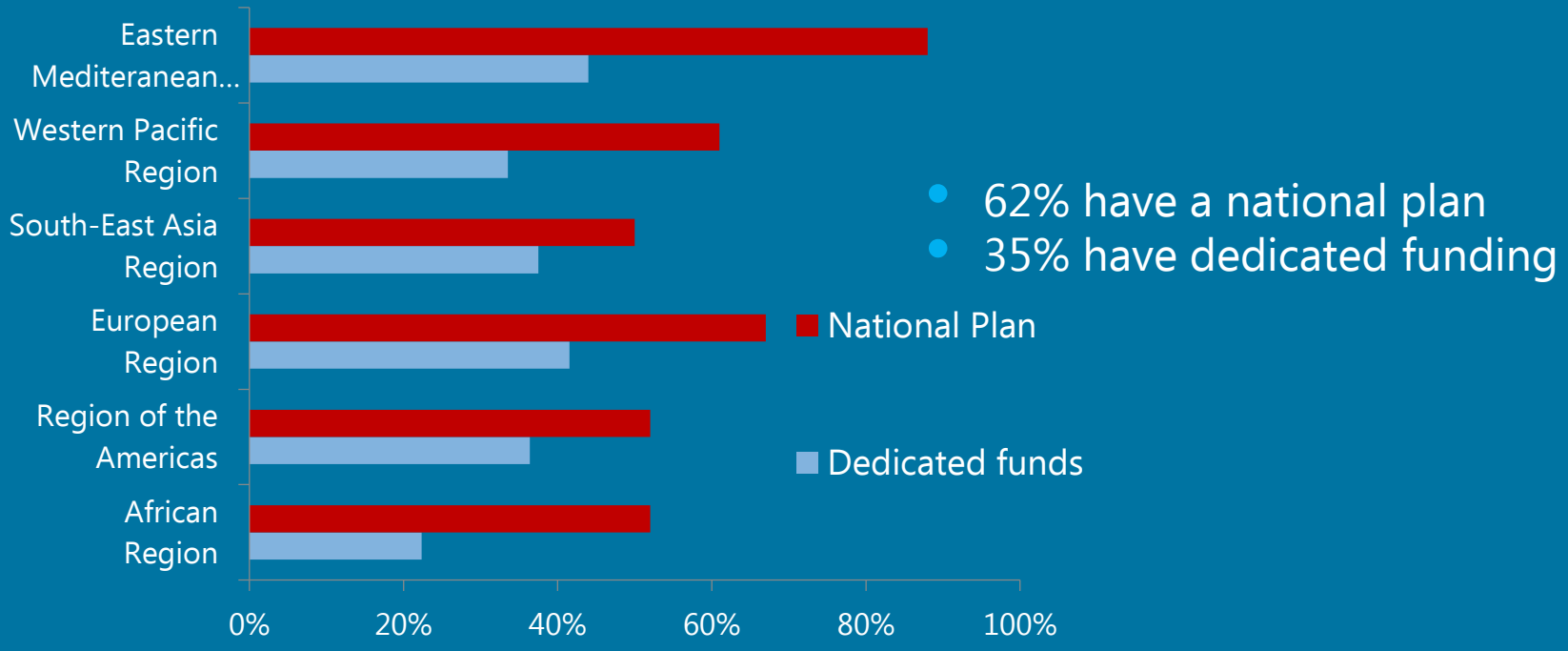


- **A 5-fold increase in 5 years**
  - 17 countries had a national plan in 2012
  - 82 countries have a national plan in 2017

The first World Hepatitis Summit and the Global Strategy have been important milestones

…yet, only 1 in 3 countries has dedicated funding

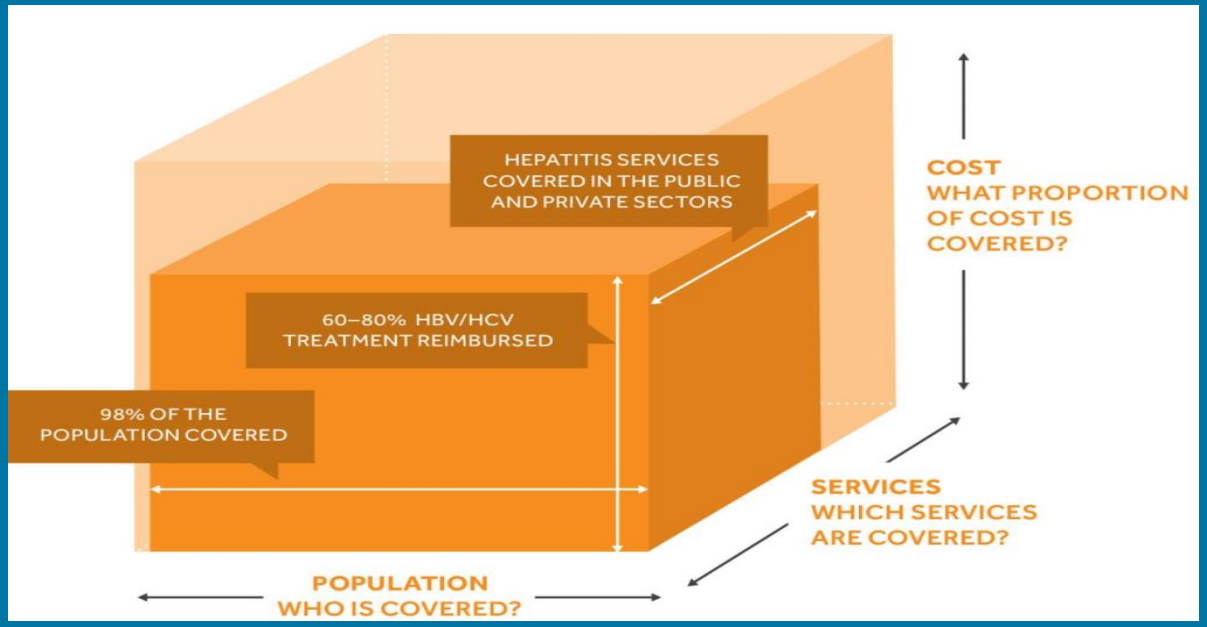
Countries with published or drafted plans and dedicated funding in 2016/17, by WHO Region



Hepatitis Elimination as Part of Universal Health Coverage (UHC): Mongolia

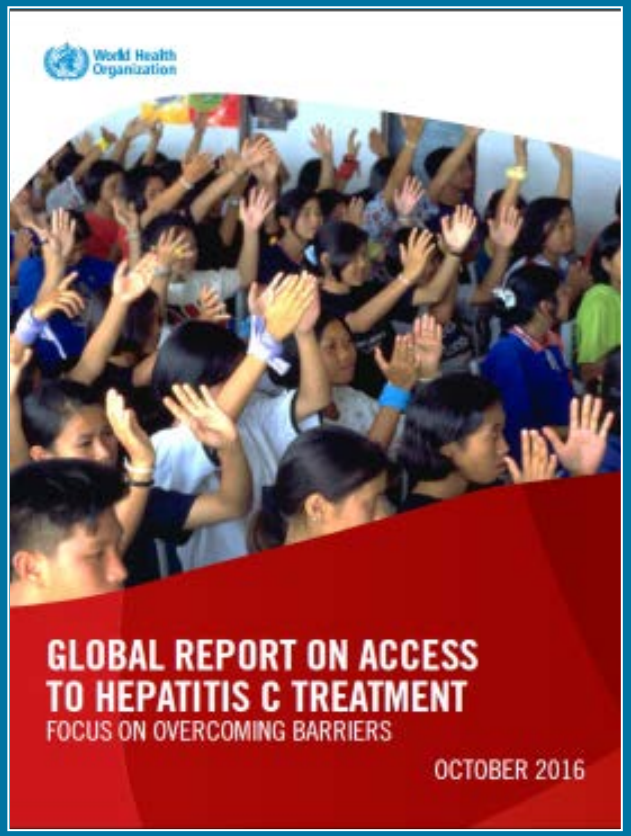
World Health Organization

- 98% population covered
- 60-80% treatment reimbursed
- Public and private sectors covered



WHO Global Report on Access to Hepatitis C Treatment

World Health Organization



Source: http://apps.who.int/iris/bitstream/10665/250625/1/WHO-HIV-2016.20-eng.pdf?ua=1

World Health Organization

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Switzerland

Thank you!

Peter Beyer | Senior Advisor | Essential Medicines & Health Products | Switzerland

www.who.int