

Viral Hepatitis Prevention Board  
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# WHO's activities, guidance, recommendations to avoid or mitigate vaccine supply shortages

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# Outline of the presentation

- **Supply shortages – the problem**
- **Trends and geography**
- **Causes of shortages**
- **Country response: reactive Vs proactive**
- **Acting strategically to secure affordable supply**
- **Demand and supply snapshots: hepatitis A and hepatitis B vaccines**

# Target 3.8: Access to Essential Medicines for All

## SDG 3 – Target 3.8

Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all.



**la Suisse manque de certains vaccins importants**  
 Pour la première fois, une pénurie de vaccins combinés de base sévit en Suisse. Ses produits sont souvent destinés aux bébés pour leur première vaccination.

**Mots-clés**  
 Office fédéral de la santé publique (OFSP)  
 Avec la Trilogie du monde

**FRANCE**  
**Pénurie de vaccins pédiatriques : "À quel point profite le crime ?"**  
 Certains vaccins sont presque introuvables en région parisienne. Le DT-Polio, obligatoire pour les enfants qui vont rentrer à l'école ou à la crèche, en fait partie. Des parents commencent à s'inquiéter.

**Acute BCG vaccine shortage: Denying newborns precious gift of life**  
 ASIF CHAUDHURY — UPDATED JUN 03, 2015 08:20AM

**SUBJECT: REQUEST FOR AID TO GET VACCINES FOR LITHUANIAN NATIONAL IMMUNISATION PROGRAMME**  
 Dear Ms Jakah,

The Ministry of Health of the Republic of Lithuania would like to inform you that our country is facing shortage of BCG (tuberculosis) and Diphtheria, Tetanus Pertussis (acellular), Poliomylitis, Haemophilus influenza type B vaccine (DTaP-IPV-Hib) because of difficulties in receiving the planned shipments.

**World Health Organization**  
 REGIONAL OFFICE FOR Europe

**Organisation mondiale de la Santé**  
 BUREAU RÉGIONAL DE L'Europe

## SAGE Recommendation April 2016 on “Pre-empting and responding to vaccine supply shortages\*"

## Resolution 69.25 – WHA – May 2016

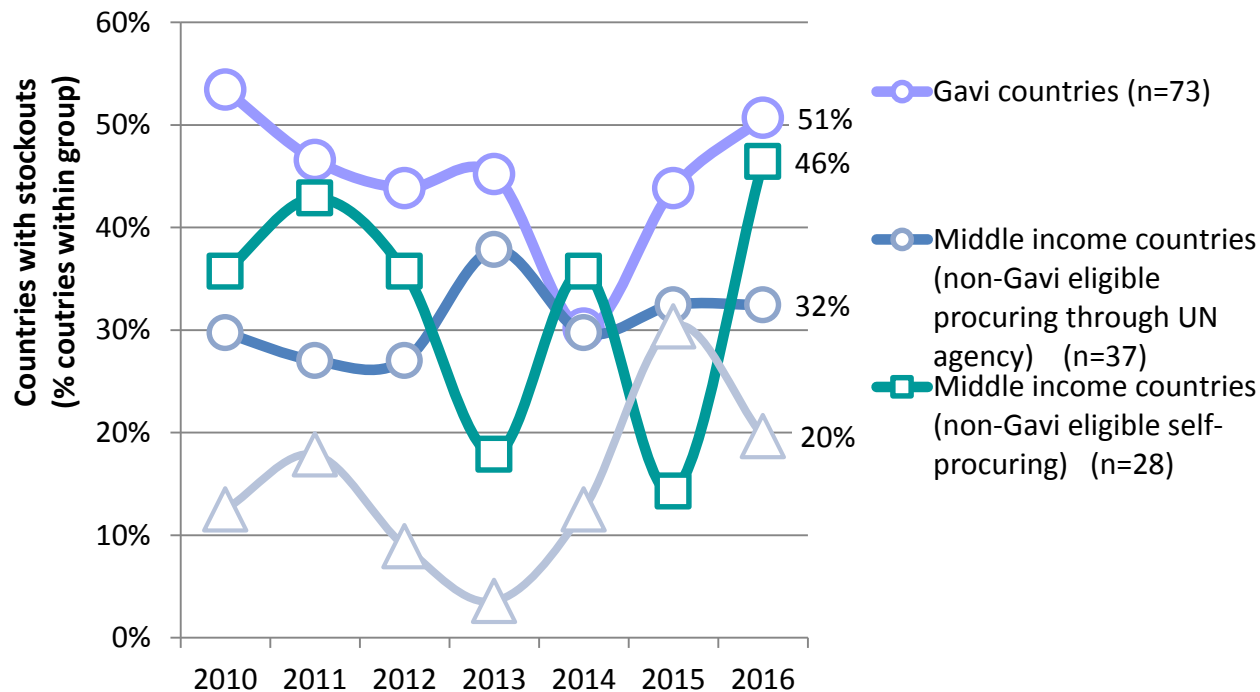
### “Addressing the Global Shortage of Medicines and Vaccines”\*\*\*

\* <http://www.who.int/wer/2016/wer9121.pdf?ua=1>

\*\* <http://apps.who.int/medicinedocs/documents/s22423en/s22423en.pdf>

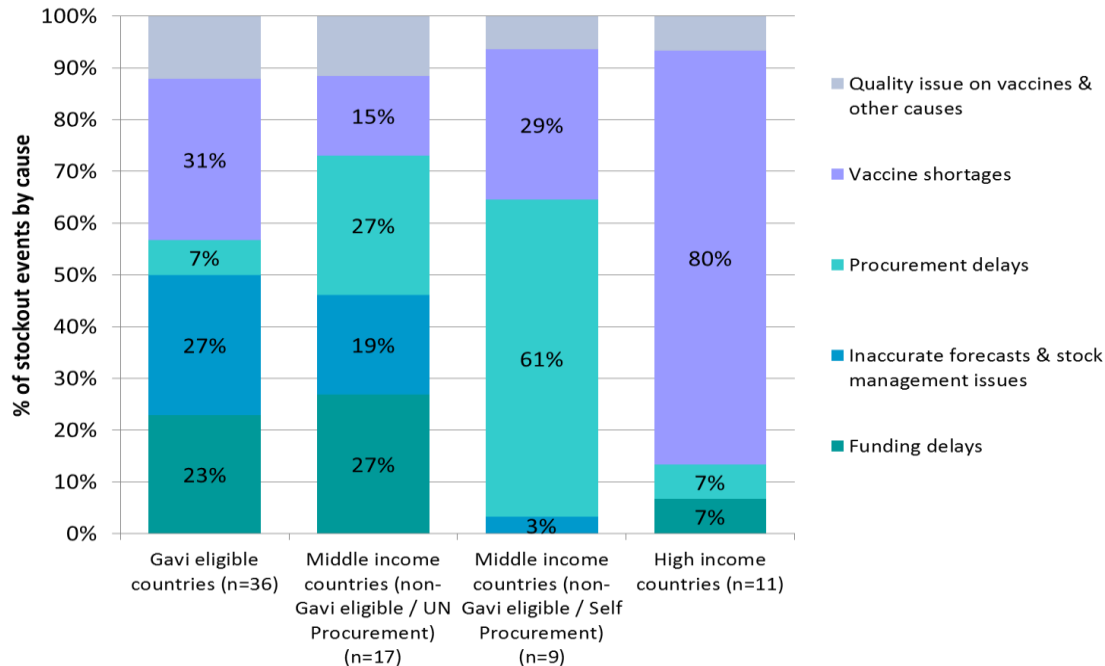


## Stock-out trends: countries across all income level are affected



❖ **20% of high income countries reported facing stock-outs in 2016**

# Stock-outs causes: vary depending on income & procurement group

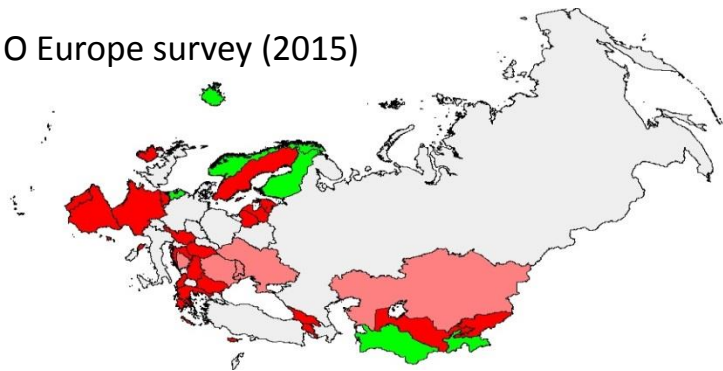


- ❖ Overall, 66% of national level stockouts due to in-country challenges
- ❖ Procurement delay and vaccine shortage are important factors for MICs
- ❖ For high income countries, supply side vaccine shortages are causing 80% of stock-outs

# Supply shortages in Euro Region:

- ALL income groups affected
- Self-procuring MICS – at higher risk
- 15 out of 25 vaccines in shortage / at risk

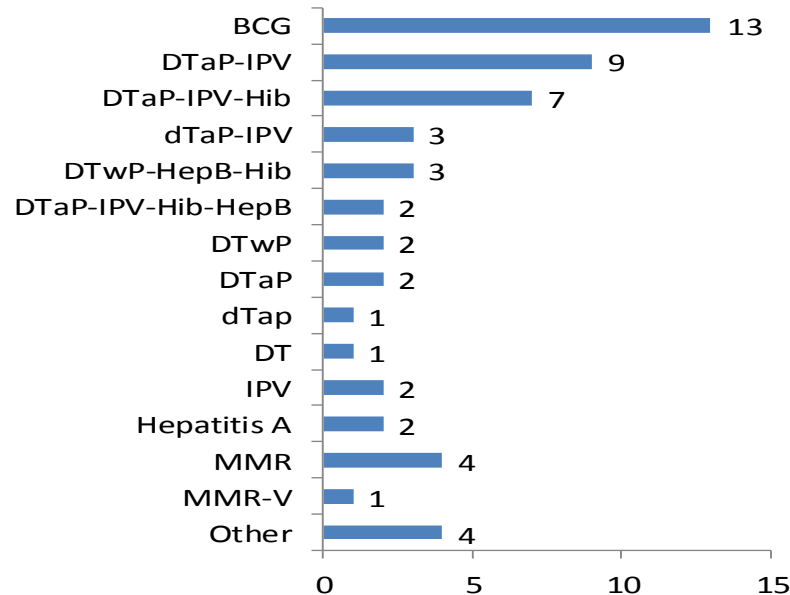
WHO Europe survey (2015)



Regional shortages (2017)

Hepatitis A  
Hepatitis B  
Td

## 28/53 WHO Europe Member States facing shortages, 2015





# Country response to shortages:

## • Reactive

- ❖ Suspended immunization for 1–4 month (HUN, IRE, LTU)
- ❖ Identified alternative suppliers/addressed regulatory barriers
- ❖ Mutual support (BUL/TUR, CRO/NOR)
- ❖ Switched to new products (penta > hexa > tetra)
- ❖ Modified the schedule (HUN, BUL, ROM, FRA)
- ❖ Used products off-label (low antigen level)

## • Proactive

- ❖ Risk assessment & response options (European Center for Disease Control/European Commission Health Security Committee)
- ❖ Vaccine supply security strategy (FRA)
- ❖ Procurement procedure changed (BUL, CRO, LTU)



# Global commitment to securing access to vaccines: WHA resolutions and access strategies

## World Health Assembly – Resolution 69.25, May 2016

*URGES Member States **to develop strategies** to forecast, avert or reduce shortages/stockouts ...*

*CALLS upon manufacturers, wholesalers, global, and regional procurement agencies... **to contribute to global efforts** to address the challenges of medicines and vaccines shortages, including through participation in notification systems;*

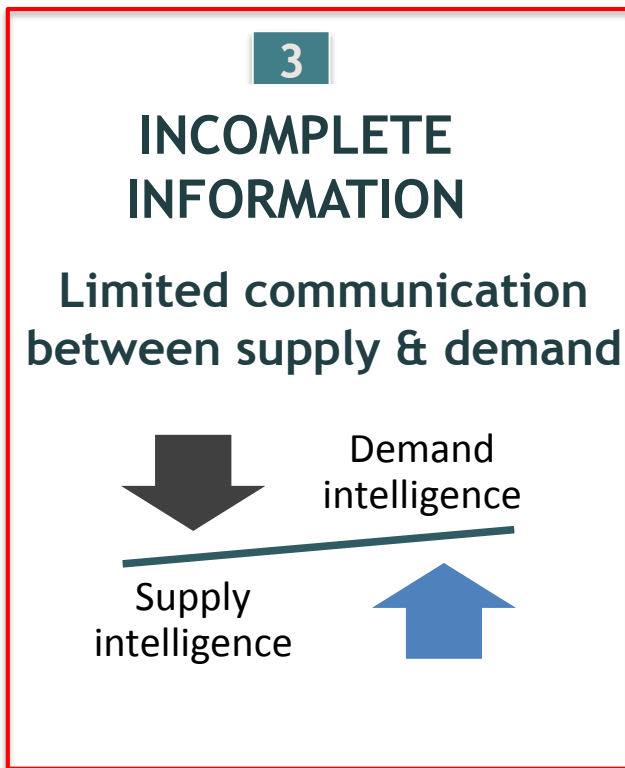
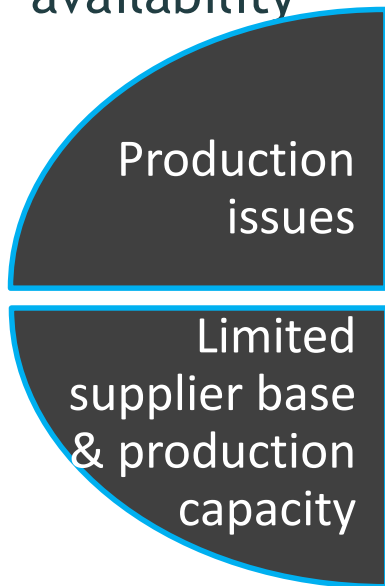
*REQUESTS DG to “**develop technical definitions**, as needed, for medicines and vaccines shortages and stockouts;*

***Assess the magnitude and nature of the problem** of shortages &  
**Develop a global medicine shortage notification system** to better detect and understand the causes of shortages*

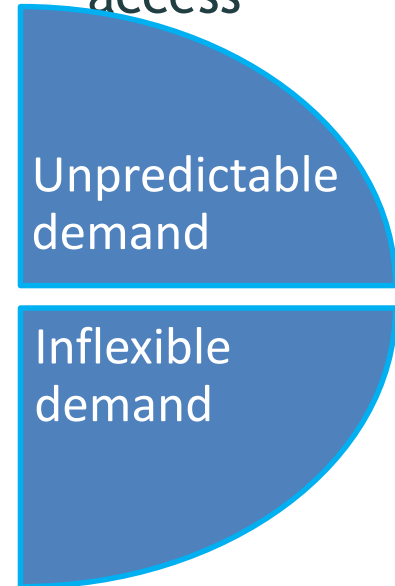


# There are various causes of shortages

## 1 SUPPLY Factors limiting availability



## 2 DEMAND Factors limiting access



# Acting strategically to secure affordable supply

*During the last two decades public procurement ..... has evolved from a clerical signoff-ridden set of activities to a strategic tool **to enhance efficiency** in public organizations, **to regulate markets** and **promote sustainable development** (OECD)*

Goal: Alligning and securing supply to reach health objectives

## SECURING SUPPLY

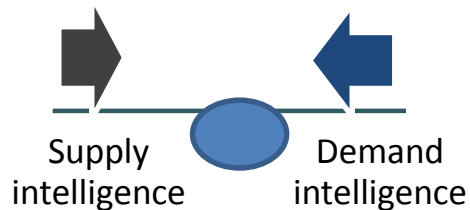
1

R&D support  
Manufacturing guidelines  
Production capacity  
Technology transfer  
Prequalification (PQ)  
Producing country NRAs

3

## COMMUNICATION

Risk notification &  
information exchange



In-country & Regional/Global

## 2 PREDICTABLE DEMAND

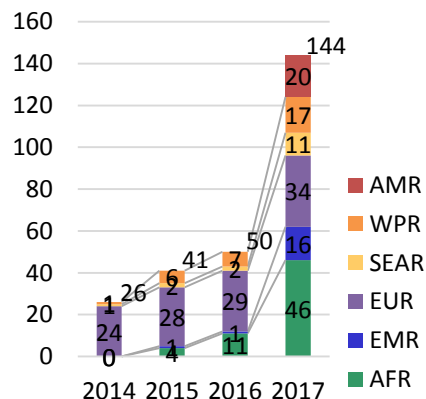
Policy setting: EVAP/NIP  
Decision making: TAGs  
Strategic planning: cMYP  
Forecasting: Multi-year  
Budgeting: Annual/MTF  
Regulatory frameworks: PQ/MR  
Procurement: Efficiency/Effectiveness  
Purchasing power: Transparency + joint procurement  
Rational use / Managing stock risks

# New developments at Global level

## Improving vaccine market knowledge

### GVAP Vaccine Price & Procurement Report 2017

- 144 countries shared price data
- 3.2 billion doses / 73 manufacturers
- Vaccine prices are stable or declining



### MARKET UPDATE BCG VACCINE

#### Key Takeaways

- For 2017, BCG vaccine supply is estimated to be 1.5 times greater than forecasted demand. This excess supply is measured given the instability of the manufacturing process and is important progress from the restricted supply situation in recent years.
- However, demand flexibility is limited due to product registration constraints and supply is still concentrated, with a few large suppliers with prequalified products serving most countries. Consequently, shortages may still occur.

#### QUICK STATS

NUMBER OF PRODUCTS  
1  
TOTAL NUMBER OF SUPPLIERS  
19  
2017 ESTIMATED MAXIMUM GLOBAL SUPPLY  
~350M doses  
2017 KINGSTON GLOBAL DEMAND  
~350M doses  
2015 REPORTED PRICE RANGE  
US \$0.04-\$15.00 (Median: \$0.52)

#### Market highlights

Over ten years (2005–2015), short duration stock-outs of BCG (maximum 1.5 months) have been reported across all regions, income groups and procurement methods. The African region, low income countries (LICs) and lower middle income countries (LMICs) were most affected. In 2014 and 2015, average stock-out duration increased. Stock-outs seem to be caused by several factors: production issues, countries having only one product registered, timely availability of financing (national or external), procurement shortcomings, and inefficient vaccine management.

#### Global demand

Annual global demand is forecasted at ~350M doses according to a model based on country reported DTP schedule, UN Population Division (UNPD) population, WHO/UNICEF estimated coverage, 50% wastage, and historical procurement data. Information on past country purchase shows that countries may be over-purchasing BCG, possibly due to actual wastage >50%, large country stock, or country target population greater than UNPD

estimates. The greatest difference in forecasted demand and historical procurement is seen for self-purchasing LMICs.

#### Global supply

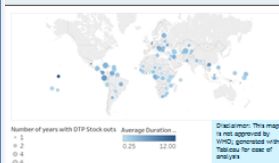
Between 2013 and 2015, manufacturing issues for most prequalified (PQ) suppliers led to temporary reduced production or suspension of production. Additionally, some non-PQ manufacturers entered the market. Nevertheless, supply increased significantly in 2016, as some of the manufacturers' production issues were resolved and one new supplier, Generalized, was PQ'd. In 2017, supply is estimated to reach ~350M doses from 19 suppliers. The suppliers can be split into two groups: 13/19 suppliers with PQ'd products that can reach 184 countries (86% of WHO member states) that accept UN procurement or have one of the PQ products registered and 2/19 suppliers with non-PQ'd products that can serve 32 countries where they have product registered. In 2017/2018, these manufacturers are expected to be back online and additional capacity could be made available from one other currently active manufacturer.

#### CURRENT BCG VACCINE MANUFACTURERS BY PQ STATUS



### D&T Advisory Group: Review of availability of D&T vaccines in the context of new policy recommendations

#### Availability of D&T vaccines



Number of years in which country experienced DTP stock-outs and average duration of stock-outs (months), 2002-2015. Source: WHO/UNICEF, JPI, Data-aid.

Vaccine	Countries with DTP coverage (n=15)	Signed record (n=15)	Duration DTP (months) (n=15)	Signed record (n=15)
DTP	19.7	30 (2015)	2.6	3.8 (2014)
TT	9.9	15 (2015)	2.5	3.7 (2014)

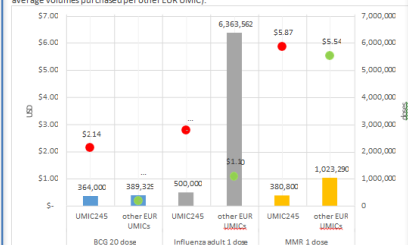
- Several stock-outs of DTP and TT over the past decade
- AFR and AMR regions and middle income groups disproportionately affected
- EURO region survey 2015 - Shortages of D&T containing products: 29 countries
- ECDC reports no availability of the TT and Td in emergency rooms & for refugees
- Reported supply constraints from suppliers prioritising combination products

### V3P Country fact sheet

#### MICs/SEEHN countries:

- Analysis of reported vaccines
- Review existing manufacturers
- Review available presentations
- Prices paid by country, compared to the range of prices paid by other countries

Chart 1.1. UMIC245 prices (red dots) in 2016, in USD, that are above WAP for other UMICs in EUR (green dots). (Column graph shows purchase volumes in number of doses for UMIC245 and corresponding average volumes purchased per other EUR UMIC).



# A quick Vaccine market snap shot: SEE countries (Example)

- **Small market size (by volume):**
  - < 4% Euro; 0.24% Global
- **Low Predictability:**
  - Exclusive 1-year contracts in 5/9 countries
- **Fragmented demand:**
  - 11/18 Products used by 4 countries or less (i.e. most are new and expensive vaccines)
- **Limited competition:**
  - Restricted supplier base
  - Products from >10 manufacturers not procured by SEE countries
- **Diverse procurement mechanisms:** self /pooled

Vaccines by Country	ALB	BIH	BUL	CRO	MKD	MDA	MNE	ROM	SRB	Total
BCG	X	X	X	X	X	X	X	X	X	9
MMR	X	X	X	X	X	X	X	X	X	9
Td	X	X	X	X	X	X	X	X	X	9
HepB (ped)	X	X	X	X	X	X	X	X	X	9
OPV	X	X			X	X	X		X	6
DT	X	X				X	X		X	5
DTaP-Hib-IPV*		X	X		X		X		X	5
DTwP	X	X			X	X				4
DTaP-Hib-HepB-IPV*			X	X	X			X		4
DTaP-IPV*		X	X				X	X		4
HPV*				X	X	X				3
PCV*	X		X			X				3
TT		X		X	X					3
DTwP-Hib-HepB*	X					X				2
Hib		X					X			2
IPV*	X			X						2
DTaP*				X						1
Rota*						X				1
<b>Total</b>	<b>10</b>	<b>11</b>	<b>8</b>	<b>9</b>	<b>10</b>	<b>11</b>	<b>9</b>	<b>6</b>	<b>7</b>	
* - new and the most expensive vaccines										

Source: WHO V3P database

# Vaccine presentations demand analysis

Vaccine type/ formulation	Country group	Proportion (%) of countries procuring the vaccine	Proportion (%) of countries procuring specific vaccine presentations			
			pfs	1d amp/vial	2d amp/vial	10 d amp/vial
HepA (ped)	EUR	6/34 (18%)	5/6 (83%)	1/6 (17%)	-	-
	EUR UMIC	3/13 (23%)	2/3 (67%)	1/3 (33%)	-	-
	SEEHN	1/8 (13%)	1/1 (100%)	-	-	-
HepB (ped)	EUR	26/34 (76%)	8/26 (31%)	13/26 (50%)	1/26 (4%)	5/26 (19%)
	EUR UMIC	11/13 (85%)	1/11 (9%)	7/11 (64%)	1/11 (9%)	3/11 (27%)
	SEEHN	7/8 (88%)	1/7 (14%)	6/7 (86%)	-	-

Source: WHO V3P database

# Supplier base for Hepatitis A and Hepatitis B vaccines in SEEHN countries, 2016

Vaccine type	Country group	Manufacturers reported
HepA (adult)	Reported by SEEHN	<ul style="list-style-type: none"> <li>• Sanofi Pasteur</li> </ul>
	Others reported by EUR but not SEEHN	<ul style="list-style-type: none"> <li>• GSK*</li> <li>• Vector-BiAlgam</li> </ul>
HepA (ped)	Reported by SEEHN	<ul style="list-style-type: none"> <li>• Sanofi Pasteur</li> </ul>
	Others reported by EUR but not SEEHN	<ul style="list-style-type: none"> <li>• GSK*</li> <li>• Merck</li> </ul>
HepB (adult)	Reported by SEEHN	<ul style="list-style-type: none"> <li>• GSK*</li> <li>• LG Life Sciences*</li> <li>• Merck</li> </ul>
	Others reported by EUR but not SEEHN	<ul style="list-style-type: none"> <li>• Centro de Ingenieria Genetica y Biotecnologia*</li> <li>• Mikrogen</li> </ul>
HepB (ped)	Reported by SEEHN	<ul style="list-style-type: none"> <li>• GSK*</li> <li>• LG Life Sciences*</li> </ul>
	Others reported by EUR but not SEEHN	<ul style="list-style-type: none"> <li>• Janssen*</li> <li>• Mikrogen</li> <li>• Sanofi Pasteur MSD</li> <li>• Serum Institute of India*</li> </ul>

Source: WHO V3P database

\*WHO pre-qualified products).



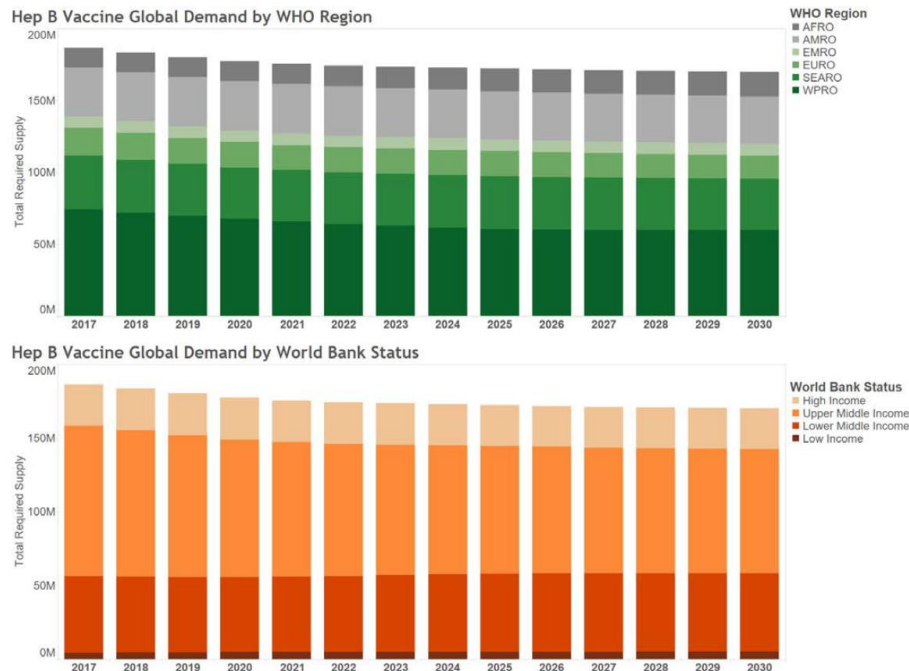
# Hep B demand & supply by WHO region

## Demand

- **Global demand < 200M doses**, declining from 2017 to 2030); China ~50-65M doses (1/4 of demand)
- If low-income countries introduce a birth dose the volumes required will be significant

## Supply

- **Global supply capacity >450M doses**
- 7 WHO prequalified suppliers
- 2 Suppliers have LTAs with UNICEF (~20M doses)



Source: Global Vaccine Market Model (GVMM) Demand Module, Linksbridge, SPC, Bill & Melinda Gates Foundation funded project January 2017

# Hepatitis A vaccines shortages – 2017-2018

## Limited information on demand and supply

### • Supply

- ❖ **5 Manufacturers**
- ❖ 2 WHO PQd manufacturers
- ❖ 3 manufacturers authorised in EU
- ❖ **1 Manufacturer discontinued in 2014 due to quality issues**
- ❖ **Manufacturing delays**

### • Demand

- ❖ **Expanding demand over 5 yrs\*:**
- ❖ **2012-4 Countries**  
GRC, ISR, KAZ, TUR
- ❖ **2016-14 Countries**  
ARM, CYP?, ESP, FIN, FRA, GRC, ISR, ITA, KAZ, RUS, SMR, SVN, TUR, UZB
- ❖ **Low demand visibility** for other 39 Euro countries
- ❖ **Steady increase in global demand for outbreak control**  
(i.e. USA, Canada)

### • Information

- ❖ **Lack of information** on demand/supply evolution
- ❖ Limited communication on shortages and reasons behind

\* Source: Annual JRF reports

# Thank you!

# Extra slides

# WHO prequalified Hepatitis B vaccines

Manufacturer/MA Holder	WHO pre-qualified	EMA	
GSK (Belgium)	<a href="#">Engerix</a>	Engerix	1; 10; 20
LG Life Sciences (Republic of Korea)	<a href="#">Euvax B</a>		1; 2; 6; 10
Centro de Ingeniería Genética y Biotecnología (Cuba)	<a href="#">Heberbiovac HB</a>		1; 10
PT Bio Farma (Persero) (Indonesia)	<a href="#">Hepatitis B Vaccine Recombinant</a>		Uniject
Serum Institute of India Pvt. Ltd.	<a href="#">Hepatitis B Vaccine (rDNA) (Paediatric)</a> <a href="#">Hepatitis B Vaccine (rDNA) (Adult)</a>		1; 10 1; 10
Janssen Vaccines Corp. (Republic of Korea)	<a href="#">Hepavax-Gene</a>		10
Shantha Biotechnics Ltd (India) (Sanofi)	<a href="#">Shanvac-B</a>		1; 2; 6; 10
Merck Sharp and Dohme, B.V. Waarderweg, 39 2031 BN Haarlem The Netherlands		HBVaxPro	

# WHO prequalified Hepatitis A vaccines

Prequalified	Type	Commercial Name	Pharmaceutical Form	Present ation	No. of Doses	Manufacturer	Responsible NRA
19/07/2013	Hepatitis A (Human Diploid Cell), Inactivated (Adult)	<a href="#">Havrix 1440 Adult</a>	Liquid: ready to use	Vial	1	GlaxoSmithKline Biologicals SA	Federal Agency for Medicines and Health Products
19/07/2013	Hepatitis A (Human Diploid Cell), Inactivated (Paediatric)	<a href="#">Havrix 720 Junior</a>	Liquid: ready to use	Vial	1	GlaxoSmithKline Biologicals SA	Federal Agency for Medicines and Health Products
22/12/2017	Hepatitis A (Human Diploid Cell), Inactivated (Adult)	<a href="#">HEALIVE</a>	Liquid: ready to use	Vial	1	Sinovac Biotech Co. Ltd	Chinese Food and Drug Administration
22/12/2017	Hepatitis A (Human Diploid Cell), Inactivated (Paediatric)	<a href="#">HEALIVE</a>	Liquid: ready to use	Vial	1	Sinovac Biotech Co. Ltd	Chinese Food and Drug Administration

Source: [http://www.who.int/immunization\\_standards/vaccine\\_quality/PQ\\_vaccine\\_list\\_en/en/](http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/)