International Federation
of Pharmaceutical
Manufacturers & Associations

IFPMA

# *International Federation of Pharmaceutical Manufacturers and Associations' (IFPMA) and the Decade of Vaccines*

## SAGE update

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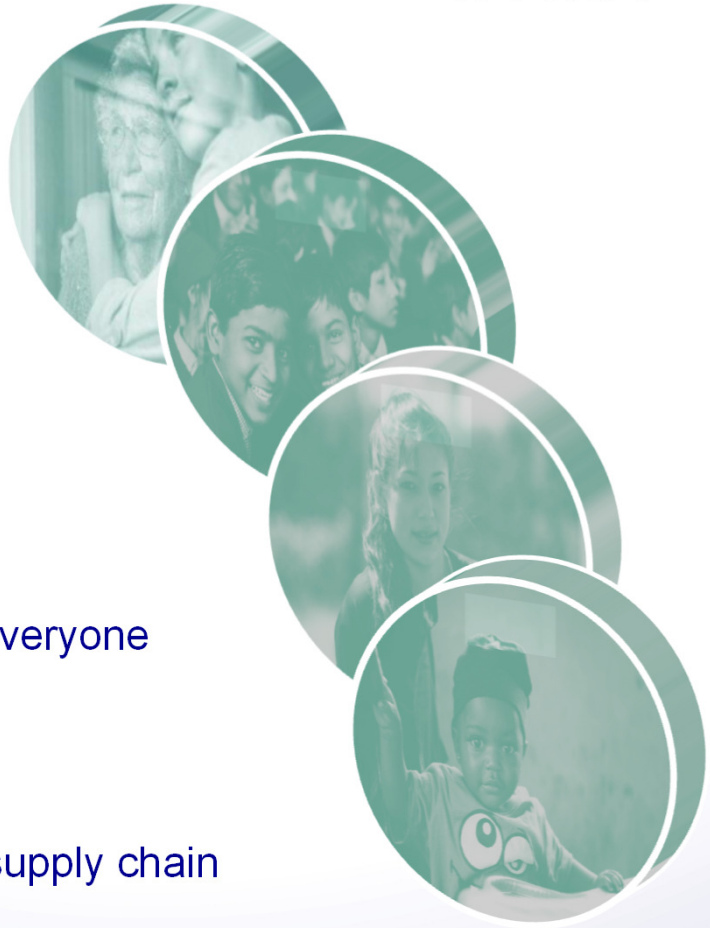
18 October 2017

# Outline

1. @IFPMA
2. Getting there together – IFPMA and its members' contributions to GVAP 2011-2020
3. Expand vaccine uptake and usage - IFPMA and its members' collaborations
4. Advance vaccine technologies, extend the benefit to everyone
   Innovation from R&D, to production and delivery
5. What can we all do to stabilize and secure the supply chain



# @IFPMA

**50** Years of collaboration

**+50** National and regional associations across the globe

**+30** International research-based biopharmaceutical companies

**7** Multinational, vaccines R&D companies

**15** Leading influenza vaccine manufacturers - Influenza Vaccine Supply (IVS) International Task Force

- Founded in 1968, IFPMA is a global, non-profit, non-governmental organization, representing the research-based biopharmaceutical industry.
- IFPMA has several expert committees which leverage industry expertise to develop effective approaches to global health issues.
- We collaborate with an interdependent network of organizations and stakeholders to strengthen and innovate immunization solutions.
- We have a unique role to play in the development and implementation of policies and practices from research to supply.

# *Getting there together – IFPMA and its members' contributions to GVAP*

1. Continue to develop, produce, and supply innovative and high-quality vaccines that meet countries' needs.
2. Support research and education agenda for immunization.
3. Participate in open dialogues with countries and the public sector to ensure sustainable access to current and new vaccines.
4. Continue to innovate manufacturing processes and pricing structures.
5. Support the media outreach for the Expanded Programme on Immunization to increase awareness.
6. Support rapid scale-up and adoption as new or improved vaccines emerge.
7. Develop partnerships that support the growth of manufacturing capabilities and increase vaccine supply and innovation.
8. Work in coordination with other partners on vaccine and immunization advocacy.

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# *How does IFPMA work to expand vaccine uptake and usage through collaboration?*

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1. IFPMA has a long record working with global immunization partners to contribute scientific, regulatory, and quality advice.

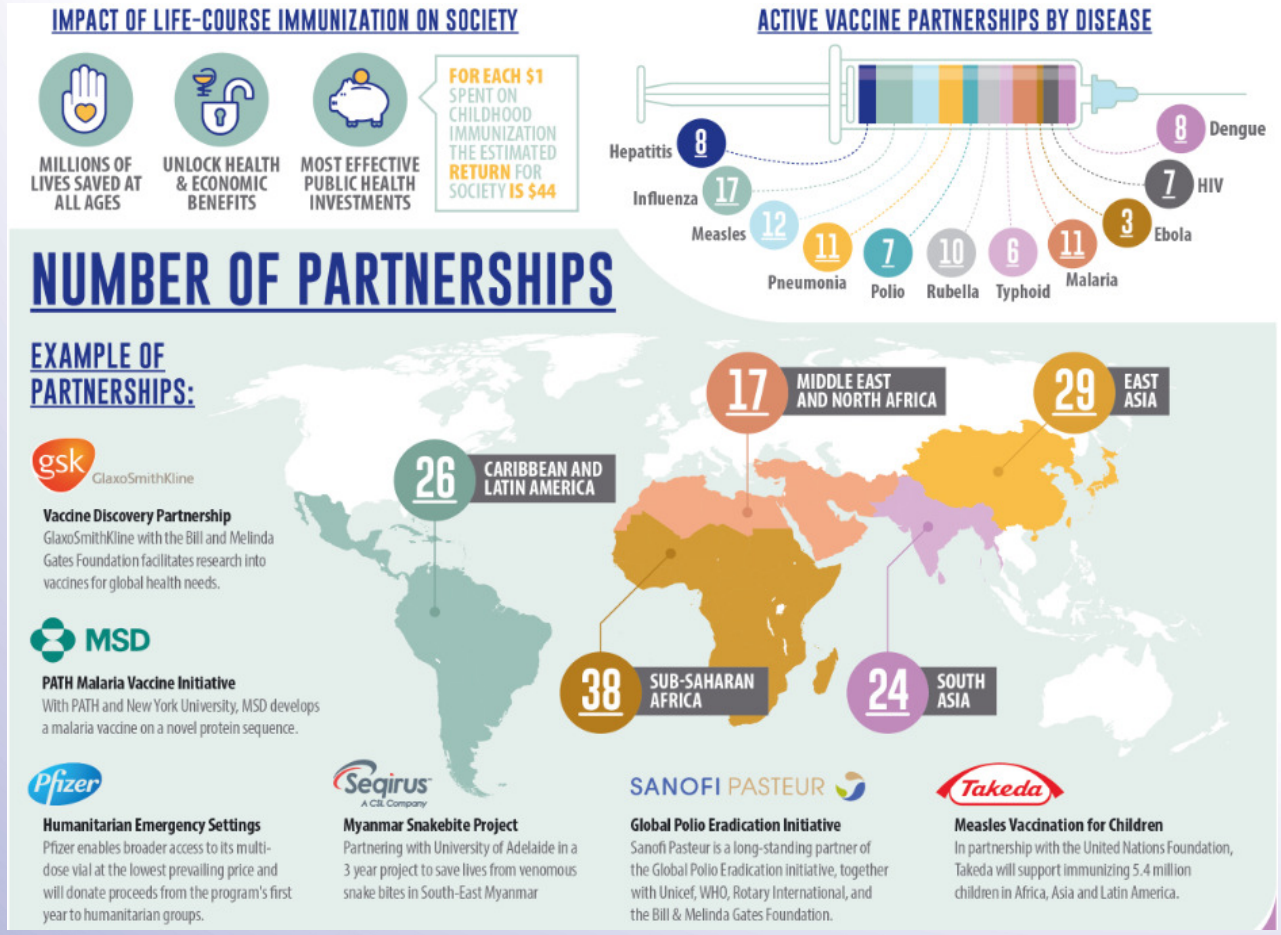
2. Regular participation, as observer, in various WHO vaccine-related activities and advisory processes, including PDVAC, ECBS, IPAQ/PSPQ SC, IVIR-AC, GVSI, WHO PQT, and SAGE.

3. Since 2000, IFPMA and its members has worked in partnership with Gavi, the Vaccine Alliance, seating at the Board and Program & Policy Committee

- Participated in over 50 WHO/partners meetings and consultations in 2016 (id. in 2017).
- Key engagements include:
  - WHO PQ financing model, launched since 1 January 2017
  - Humanitarian mechanism, launched since 1 May 2017
  - External evaluation of the international coordinating group (ICG) on vaccine provision mechanism
  - Shortage - Global Vaccine Market intelligence hub, definitions, global notification system
- Regulatory System Strengthening, variation management, and national registration for UN supplied PQ'ed vaccines

# *How do IFPMA members work to expand vaccine uptake and usage through partnership?*

- There are over 40 active partnerships for vaccines around the world involving seven innovative vaccine IFPMA member companies.




AERAS

Aeras' goal is to develop, test, characterize, license, manufacture and distribute at least one new TB vaccine within 10 years.

Gavi The Vaccine Alliance

GAVI Alliance unites public and private sectors to create equal access to new and underused vaccines for children living in the world's poorest countries.

GHIT Fund

GHIT is a product development fund for global health research and development, including a vaccine development for malaria.

IAVI

IAVI was created in 1996 and works with more than 50 partners to develop and assess candidate HIV vaccines.

Hilleman Laboratories

Hilleman develops affordable vaccines in developing countries. It aims to strengthen public health systems and immunization programs.

CEPI | New vaccines for a safer world

The Coalition for Epidemic Preparedness Innovation (CEPI) accelerates research and development of vaccines for emerging infectious diseases.

World Health Organization Pandemic Influenza Preparedness (PIP) Framework

IFPMA members provided WHO with nearly 90% of PIP funds & significantly contribute to securing pandemic doses for next pandemic.

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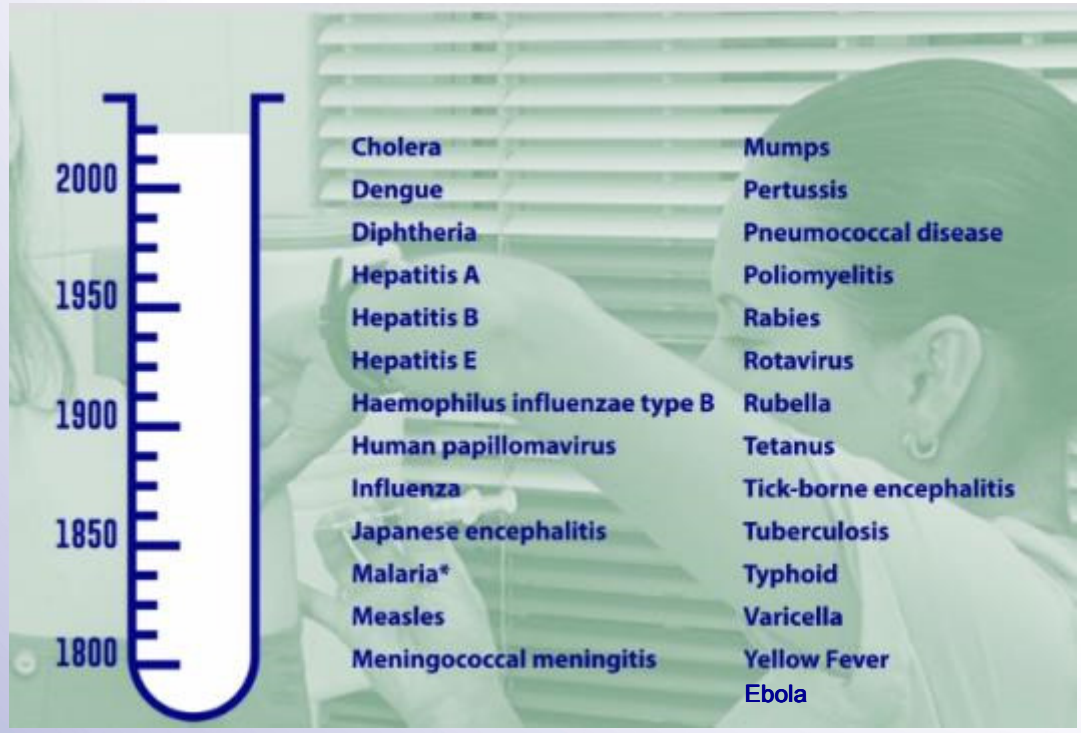
# *Advance vaccine technologies, extend the benefits to everyone - Research and development*

**27** Diseases that could be prevented by today's vaccines:




We continue to invest in innovation to address unmet public health needs*

- Borellia
- Chikungunya
- Clostridium difficile
- Dengue
- Ebola / Marburg
- Extra-intestinal pathogenic Escherichia coli
- Group A Strep
- Group B Strep
- Hand, Foot & Mouth Disease
- Hepatitis C
- HIV
- Malaria
- Norovirus
- Pseudomonas aeruginosa
- Respiratory Syncytial Virus
- Staphlyococcus aureus
- Streptococcus pneumoniae

* Non-exhaustive list of vaccine R&D

# *Advance vaccine technologies, extend the benefits to everyone - Supply chain delivery innovation*

- We apply our technical knowledge and capabilities to improve our vaccines by creating new formulations, by combining vaccines, exploring new technologies such as adjuvants, and reducing storage space.


Source: IFPMA Complex Journey of a vaccine Part II - https://www.ifpma.org/wp-content/uploads/2016/01/IFPMA-ComplexJourney-FINAL-Digital.pdf

# Controlled chain temperature (CTC)

1. IFPMA is engaged, as observer, in the IPAC working group on CTC.

2. 
- Quadrivalent HPV vaccine prequalified for CTC use in June 2016*[1]
- Oral cholera vaccine currently under review (PQ expected Q3 2017)

3. Examples of vaccines under reformulation for CTC use:
- Malaria
- Rotavirus vaccine


*[1]Source: Draft WHO CTC Strategic Roadmap

*[2]WHO IPAC CTC WG's four priority for programmatic reasons – HPV, Oral Cholera Vaccine, Tetanus Toxoid vaccine, and HepB birth dose vaccine (Source IPAC CTC WG meeting Feb 2017)

IFPMA Complex Journey of a vaccine Part II - https://www.ifpma.org/wp-content/uploads/2016/01/IFPMA-ComplexJourney-FINAL-Digital.pdf

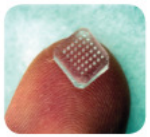
# *Optimize cold-chain impact through packaging and presentation innovation*

## Packaging optimization

1. Pfizer changed the pneumococcal vaccine presentation from a prefilled glass syringe to a single-dose vial for use in the developing countries > reduce cold chain space per dose required from 55.9cm$^3$ to 12cm$^3$.

2. GSK changed the presentation of its first-generation rotavirus vaccine to a ready-to-use liquid presentation in an oral applicator (156cm$^3$ to 85.3cm$^3$), and then developed a plastic tube presentation requiring only 17.1cm$^3$ of space per dose to store and transport.

## Presentation optimization



1. Intradermal patch

2. Microneedles

3. Disposable syringe jet injectors

IFPMA Complex Journey of a vaccine Part II - https://www.ifpma.org/wp-content/uploads/2016/01/IFPMA-ComplexJourney-FINAL-Digital.pdf



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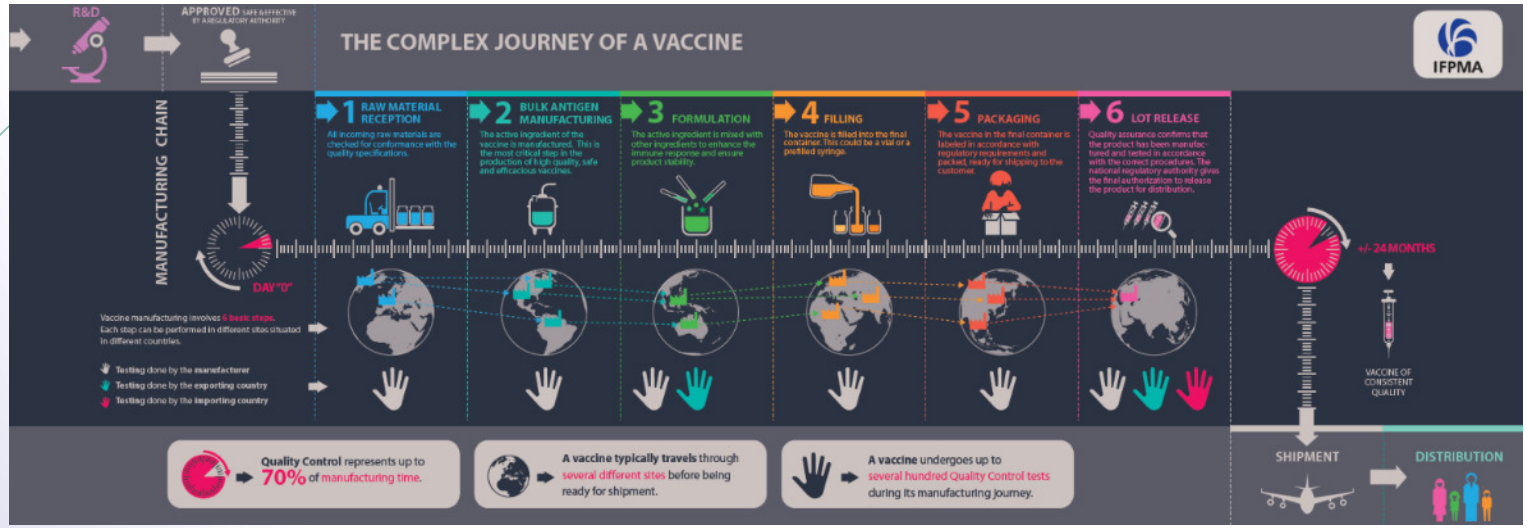
# *Stabilizing and securing the supply chain*
## *from a global manufacturing perspective*




| | Antigens | Buildings | Mfg steps | Raw Mat'ls | Test methods | Tests |
|---|---|---|---|---|---|---|
| 5 in 1* | 8 | 10 | 49 | 141 | 222 | 1265 |

- Long lead time (up to 30mo.), with up to 70% is quality control for vaccines
- Scale up production (up to 5-10yrs) with significant investments and long timelines for regulatory approval
- Diverse country specific product and packaging requirements
- Divergent regulatory requirements, notably for post-approval changes
- In vivo testing and dual or multiple batch release testing, performed by health authorities

*Source: Anders Vinther/IFPMA pre-ICDRA presentation, 2016 (Pentaxim, sanofi pasteur)

# *Best vaccines procurement and stock management methods to help ensure supply*

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## More accurate demand forecasts

Early dialogue between stakeholders including manufacturers to understand the implications of policy changes that may impact vaccines supply, e.g., mandatory

## Flexible procurement practices – in sync with vaccine scarcity and long production cycles (6-30 months to produce a vaccine)

Encourage **multi-year tenders** where legally possible to help secure supply

Include realistic tender delivery deadlines taking into account long manufacturing timelines

Encourage countries to develop a **process** in the local procurement procedure in which manufacturers can **ask questions about unclear tender specification** (e.g., delivery timeframe, shelf life, …)

Encourage **flexibility around the remaining shelf life** to make it easier for manufacturers to bid on tenders

## Limited variable contractual quantities

If tenders allow for wide variations in requested volumes (from 80% - 120% of stated volume), the best use of vaccines supply may not be achieved.

# ***Complexity of independent lot release can lead to unintended consequences on availability***

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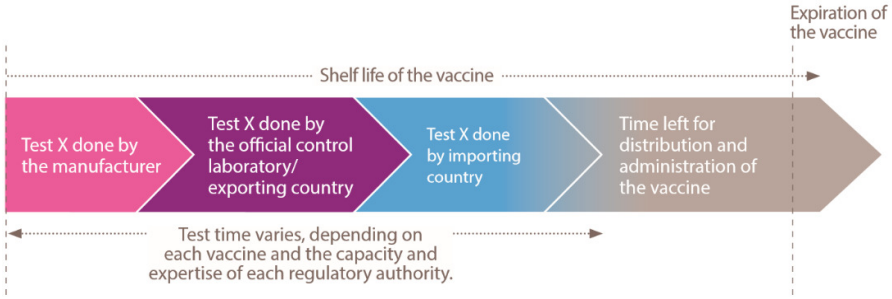
**>100** Countries receiving a vaccine with different release approaches

**~60** Official Medicines Control Laboratories (OMCL) and National Control Laboratories (NCL)

**>4** Not uncommon for a lot be tested multiple times by different NCLs




- Although there was a harmonization initiative driven by WHO (BS/10.2128), there is unfortunately not one but multiple regulations on a worldwide perspective
- Can cause vaccine shortage due to the inherent variability and long lead times of testing – particularly in the case of need for additional retesting (in vivo)
- While we recognize the public health benefits of independent lot release process, in-country agency testing for batch release can be redundant to testing and release performed by manufacturers and initial release testing agency (country of origin agency)

# *Risk-based approach to independent lot release*

- Since the implementation of the lot release regulations, vaccine technical and regulatory environment has seen major changes and evolution:
  - Improvements in sterility assurance principles
  - Implementation of Risk management (ICH Q9) and Pharmaceutical Development (QbD initiative)
  - Increase in number of cGMP inspections
  - Tremendous experience has been accumulated by the different NCL about manufacturers and established product lines

- To help ensure supply, the lot release system could still be further improved to ensure continuous application of the current system to new products / new manufacturers, while for established products, testing waivers could be considered (risk-based approach) and exploration of Mutual Recognition between agencies.

Source: IFPMA position paper on import testing https://www.ifpma.org/resource-centre/import-testing-position-papers/

# *Complexity of post-approval changes*
## *from global manufacturing perspective*

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- Post-Approval Changes (PAC) are natural and essential to the life-cycle management of a medicines or a vaccine:
  - Enhance robustness and efficiency of manufacturing process
  - Improve Quality Control techniques
  - Respond to changes in regulatory requirements
  - Respond to supply chain and suppliers change
- Regulatory processes for PAC changes differ between countries in terms of:
  - Approval timelines
  - Reporting requirements
  - Reporting categories
  - Post-approval variation content
- Example: Manufacturing capacity increase & associated changes

1 Variation for 6 Changes

Licensed in 138 countries

- Major reporting level: 62 countries
- Minor reporting level: 37 countries
- No reporting: 39 countries

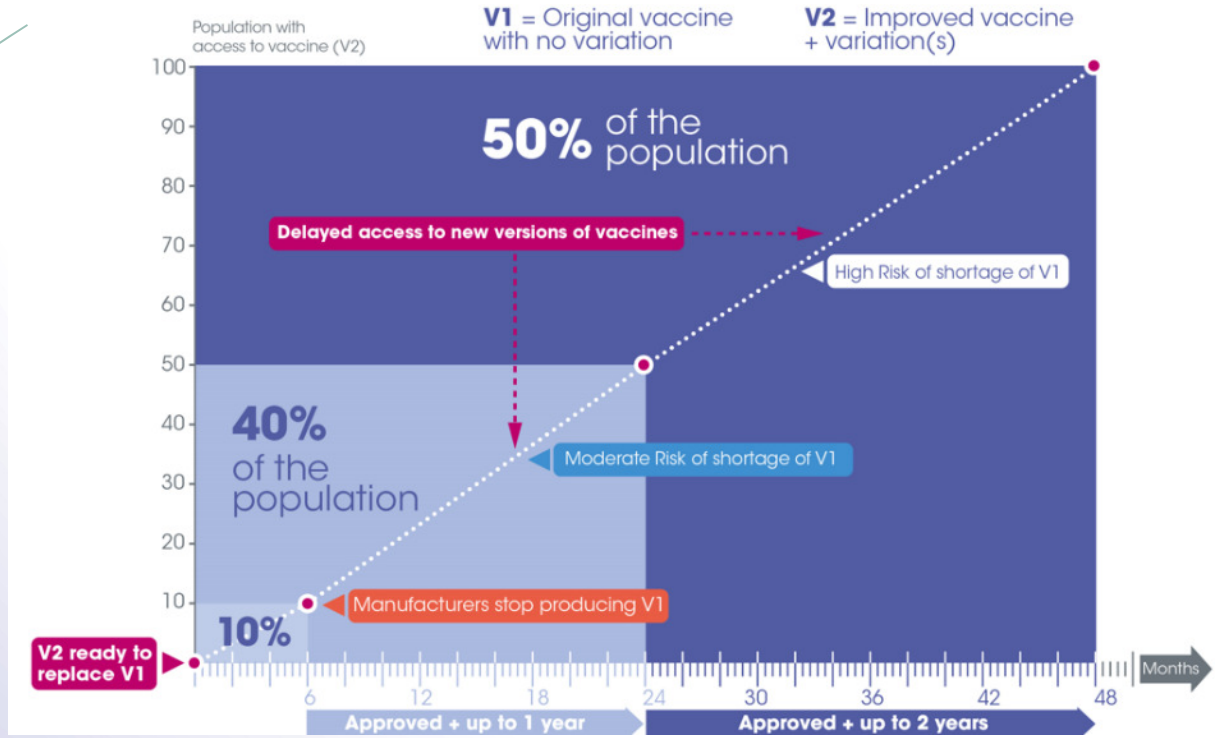
7 products impacted

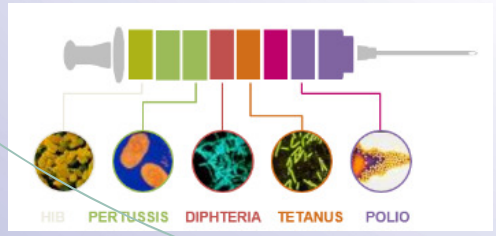
22 countries have asked 177 questions out of which 19 are different



Source: Anders Vinther/IFPMA pre-ICDRA presentation, 2016

# *Approval times, risk of shortage and inequity*




In one year: 83 batches, 55 processes. At the same time, many “versions” of the product in inventory which makes logistics a huge challenge.



Source: Anders Vinther PDA PAC iAM Workshop 2016; IFPMA Complex Journey of Vaccine, part I, https://www.ifpma.org/wp-content/uploads/2014/01/IFPMA-ComplexJourney-Part_One_2016.pdf

# *The post-approval change paradox*

cGMPs require facilities and processes to be current

Improvements are intended to reduce risks

Improvements intended to assure better availability of products

Changes in high tech industries usually happens in months

Even a simple PACs take up to 5 years for global market approval to facility/process current

Long PAC approval timelines delay risk reduction

Long PAC approval timelines hinder availability

In the pharma industry changes are measured in years



Source: Anders Vinther/IFPMA pre-ICDRA presentation, 2016

# *Risk-based approach to post-approval changes*


- Consistent, risk-based, regulatory reporting levels and requirements
- Clear and transparent regulatory assessment timelines and adherence by NRAs
- Expedite approval of certain variations of significant benefit to patients, e.g., to prevent/alleviate shortages or improve safety
- Transparency, consistency, and predictability in regulatory outcomes and decision making
- Closer harmonization and specialization of NRAs, leading to reliance and potential mutual recognition

Source: IFPMA position paper on the handling of PACs
https://www.ifpma.org/wp-content/uploads/2016/11/IFPMA-LCM-Position-Paper-vNov-2016-Final.pdf

# *What can we achieve together*

From saving one life at a time to supporting a country's long-term, immunization sows seeds for the future. Providing a better quality of life, longer and healthier lifespans, as well as lower treatment costs bring broad social and economic benefits for societal development.

Industry has a role to play in stabilizing and securing the supply chain. Todays, we need further dialogue and collaboration with the global vaccine community to find solutions on best procurement practices, risk-based approach to independent lot release, and to post-approval changes.




Source: IFPMA infographic "From shortages to sustainable supply" https://www.ifpma.org/wp-content/uploads/2017/04/Sustainable-Supply-Infographic.pdf

# *Thank you*

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