Quality of vaccines: past, present and future challenges

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Outline of presentation

- The objective
- Demand forecast
- Pathway for supply to International markets
- Need for vaccines of assured quality
- Challenges to meet PQ standards of quality including programmatic requirements
- Challenges to register vaccines in producing and receiving countries
- Proposed solutions

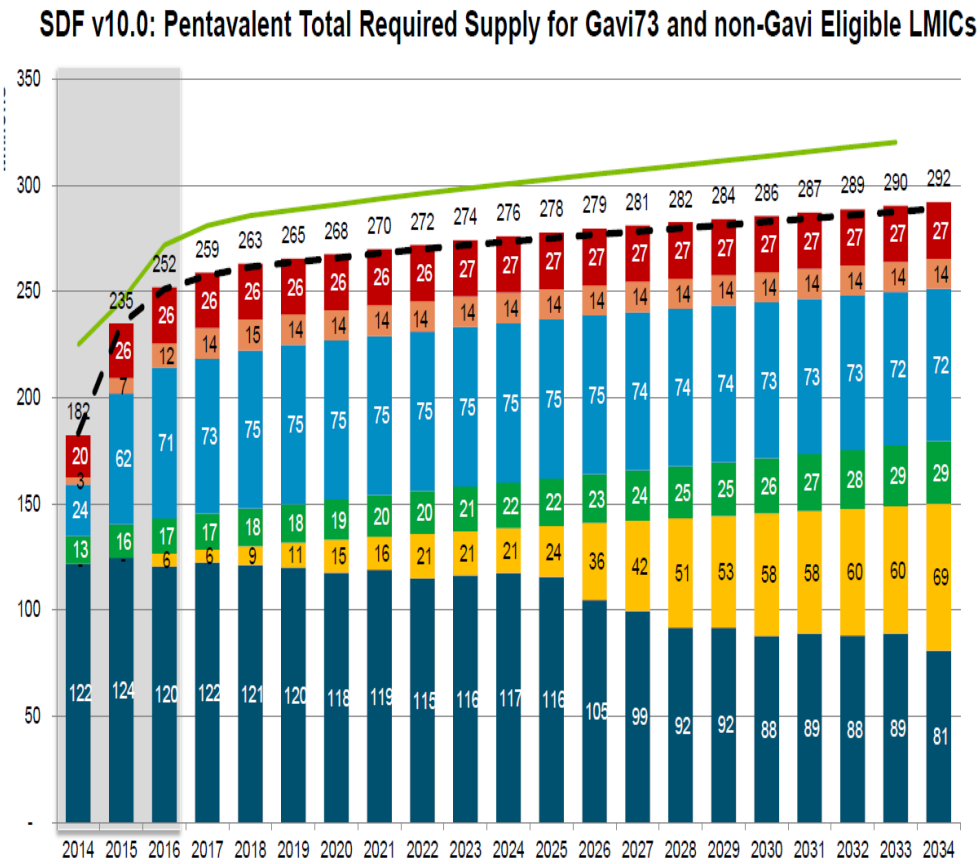
The Objective

Access for all member states to vaccines needed to fight infectious diseases of public health relevance at affordable prices. This requires enough availability and supply of vaccines of assured quality, safety and efficacy meeting the programmatic needs of countries, particularly those which are less resourced.

Demand forecast for vaccines

Demand for traditional EPI vaccines continues to be high and is increasing for some

- Pentavalent demand expected to increase rapidly in the coming years and then stabilize at approximately 300 M doses by 2034

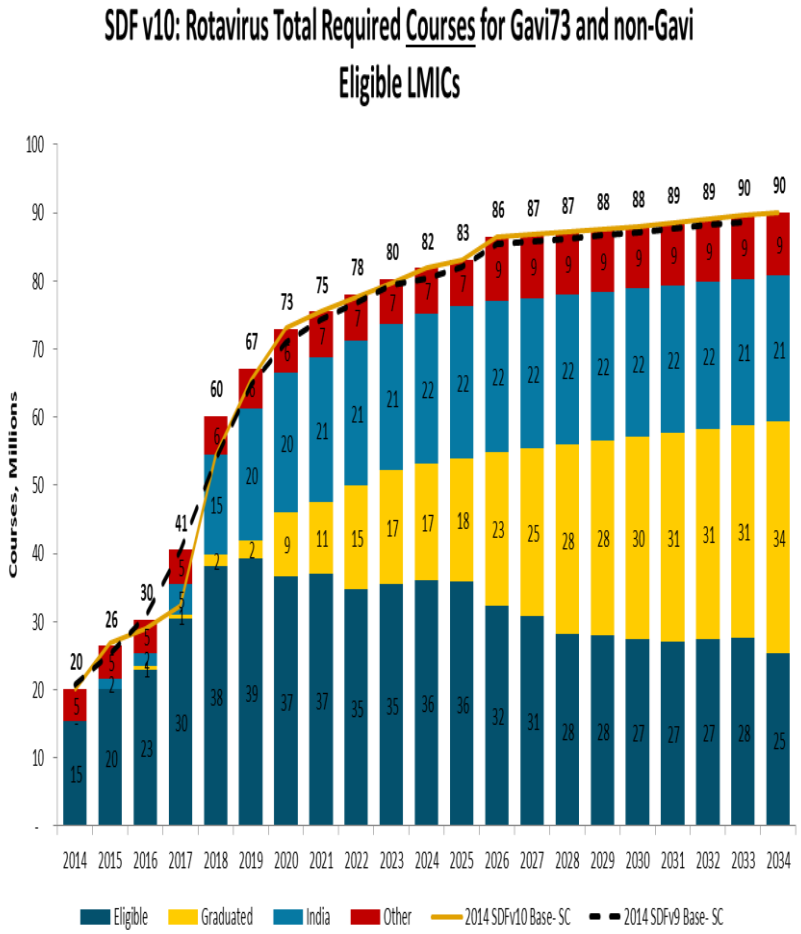


Information Source UNICEF Supply Division: Market updates presentation

Demand forecast for vaccines

Demand for newly introduced vaccines in GAVI-eligible and non GAVI-eligible LMIC

- PCV demand expected to increase from 103 M doses (2014) to 285 M doses (2034)
- Rotavirus vaccine demand expected to increase from 20 M doses (2014) to around 90 M doses (2034)
- HPV in two dose schedule expected to ramp up from around 2 M doses (2014) to around 50 M dosess (2034)



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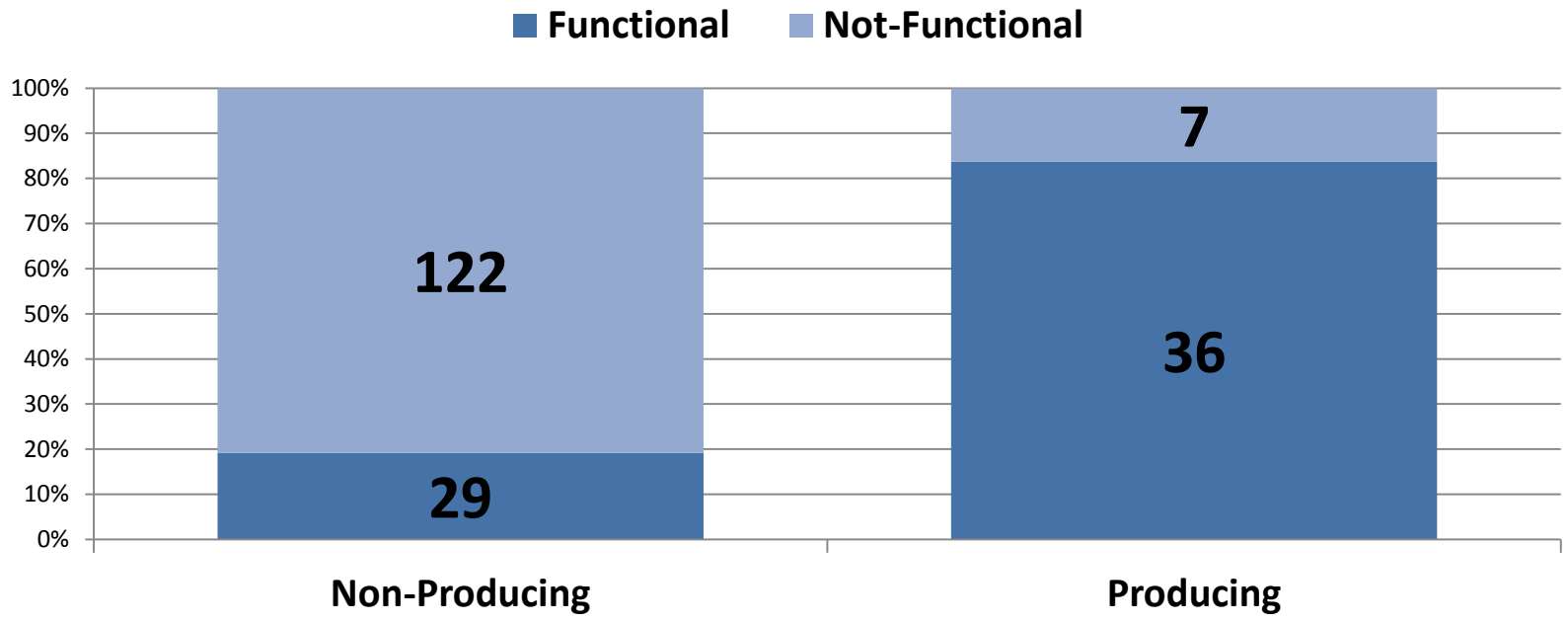
- Contribution by developing country manufacturers to the supply of vaccines currently in NIP is key to me
hea
- Add
recently introduced into the NIPs (rotavirus, pneumococcus and human papilloma virus) are needed to meet the forecasted demand

Important role to be played by DCVM members in vaccine market

Requirements to access international vaccine market

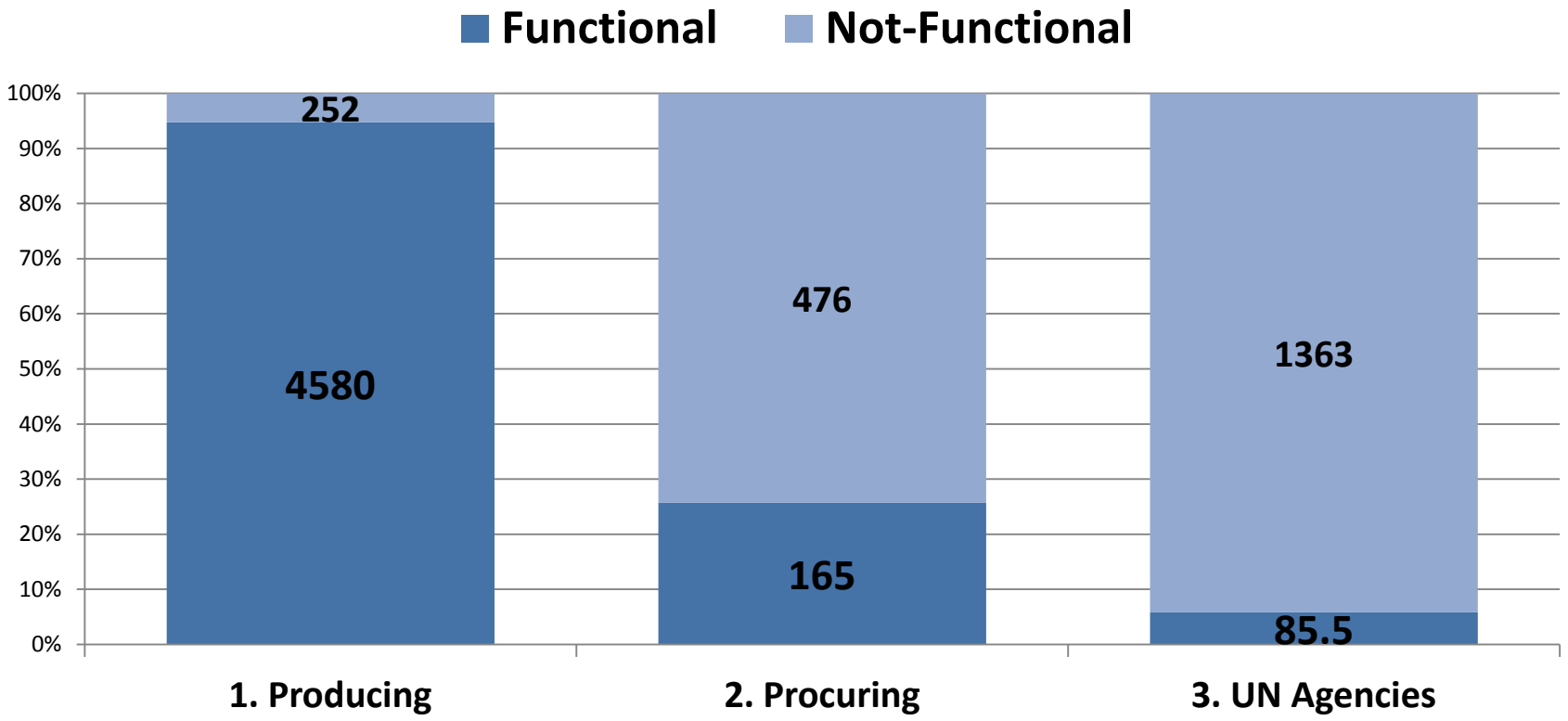
- Vaccines of assured quality ensured through
  - Functionality of the NRA in country of origin (adequate ongoing regulatory oversight) and
  - WHO prequalification
- Conditions for PQ
  - licensed in country of origin
  - meeting WHO recommendations for quality, safety and efficacy (relevant TRS documents)
  - meeting tender specifications
  - meeting programmatic needs ensured through defined PSPQ criteria

Functionality of NRAs in vaccine producing and non-producing countries as of July 2014



- 43 out 194 countries worldwide are producing human vaccines. 36 of these have functional NRAs (as assessed by WHO).
- China being the new country with a functional NRA able to supply a prequalified JE vaccine since 2013.
- Recently Mexico also achieved functionality of the NRA

Proportion of the global population living in countries with functional regulatory authorities for vaccines, 2014



- About 69.71% (4.831 billion people) live in the 65 countries, both vaccine-producing and non-producing, where there is direct oversight by a functional NRA and/ or use WHO prequalified vaccines.
- However, even in the remaining countries without functional NRAs where 30.3% of the world's population lives, supply of vaccines of assured quality to national immunization programmes is guaranteed by WHO prequalification

Past and present challenges to meet WHO_PQ standards

Quality	Incomplete dossiers, Lack of data at commercial scale No history of characterization Master and Working cell banks: Inappropriate devices: (nasal administration)
GMP	Quality systems Manufacturing process
Clinical	Lack of clinical consistency data, unclear ethical oversight Clinical trial comparator product not acceptable, lack of access to raw data and /or old data not meeting current GCP
Programmatic	Not meeting programmatic needs, eg, non -autodisable prefilled syringes, stability profile and VVM
Regulatory	National vs WHO requirements:, Test methodologies and GMP Schedules and target population, Monodose vs multidose presentation (preferred)

WHO-PQ Proposed solutions

- Programmatic suitability criteria

- Quality, safety and efficacy

- Regulatory

- Post-PQ monitoring

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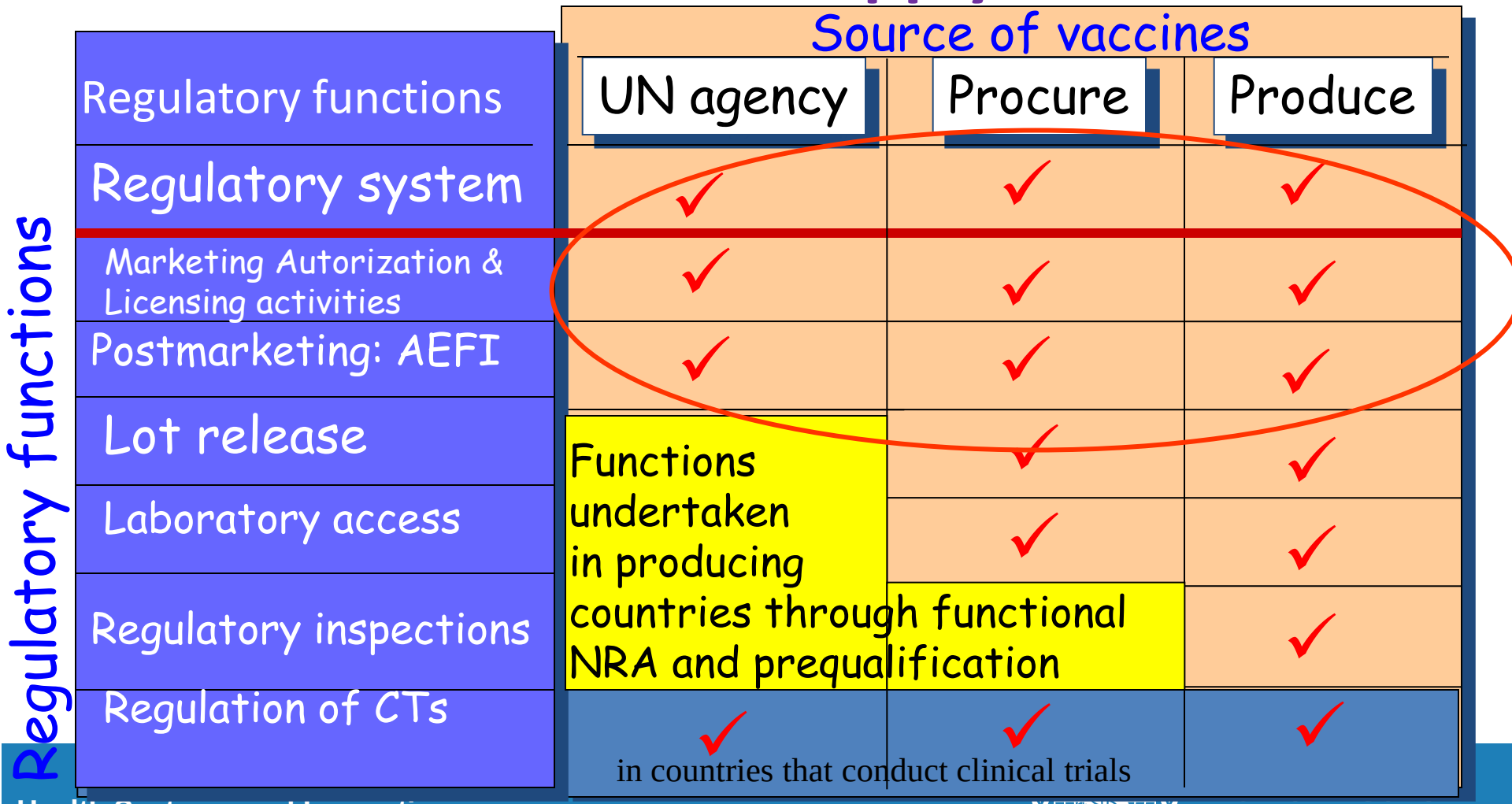
Recommended regulatory functions to be implemented according to main source of vaccine supply



CTs : Clinical trials, UN: United Nations, AEFI: Adverse Events Following Immunization

Challenges for registration of vaccines in country of origin

Licensing Of facilities	Initial license and later authorization of new buildings or upgrades of existing buildings
Local clinical trials	Registration requirements may include local clinical trials for products mostly targeted to other markets
GCP	GCP compliance for domestic clinical trials still an issue
GMP standards	GMP standards sometimes different from those internationally enforced

TIMELINES ?

Challenges for registration of vaccines iln receiving countries

Dossiers	Lack of expertise to review files, however CTD dossiers required in many countries
Testing	Vaccine samples required for testing, however tests performed are not always relevant or well done
Inspections	GMP inspections enforced by many countries in spite of lack of expertise and availability of GMP certification from country of origin, and inspections conducted by other stringent NRAs or WHO as part of PQ evaluation
Clinical trials	Local clinical trials required in spite of availability of data from trials conducted in different regions, settings and epidemiological and socio-economic conditions

Lack of provisions in regulation to enable rapid registration in case of emergency

WHO Proposed solutions

- Continue efforts to strengthen regulatory capacity further
- Advocacy of collaborative agreements with NRAs for use of expedited/facilitated procedure for registration of imported prequalified vaccines
- Joint review meetings to assist countries for review of CTD dossiers in countries where full review process is enforced
- Advocate for recognition of inspections and testing conducted by other countries through reports sharing
- Points to consider by DCVRN on requirements for local clinical trials for registration of imported vaccines
- Work towards improvement/ flexibilization of regulatory frameworks in countries
- Sustain and support networking between NRAs at global and regional levels including economic blocks

THANK YOU