

COMPLEXITY OF QUALITY CONTROL AND VACCINES MANUFACTURING

VACCINES PRODUCTION: HIGHLY COMPLEX

Increasing complexity, controls and cost to produce



MOLECULE

SMALL
MOLECULE
DRUGS

- Small, well characterized molecules
- Solid processes & experience
- Limited quality control burden
- Lower production costs



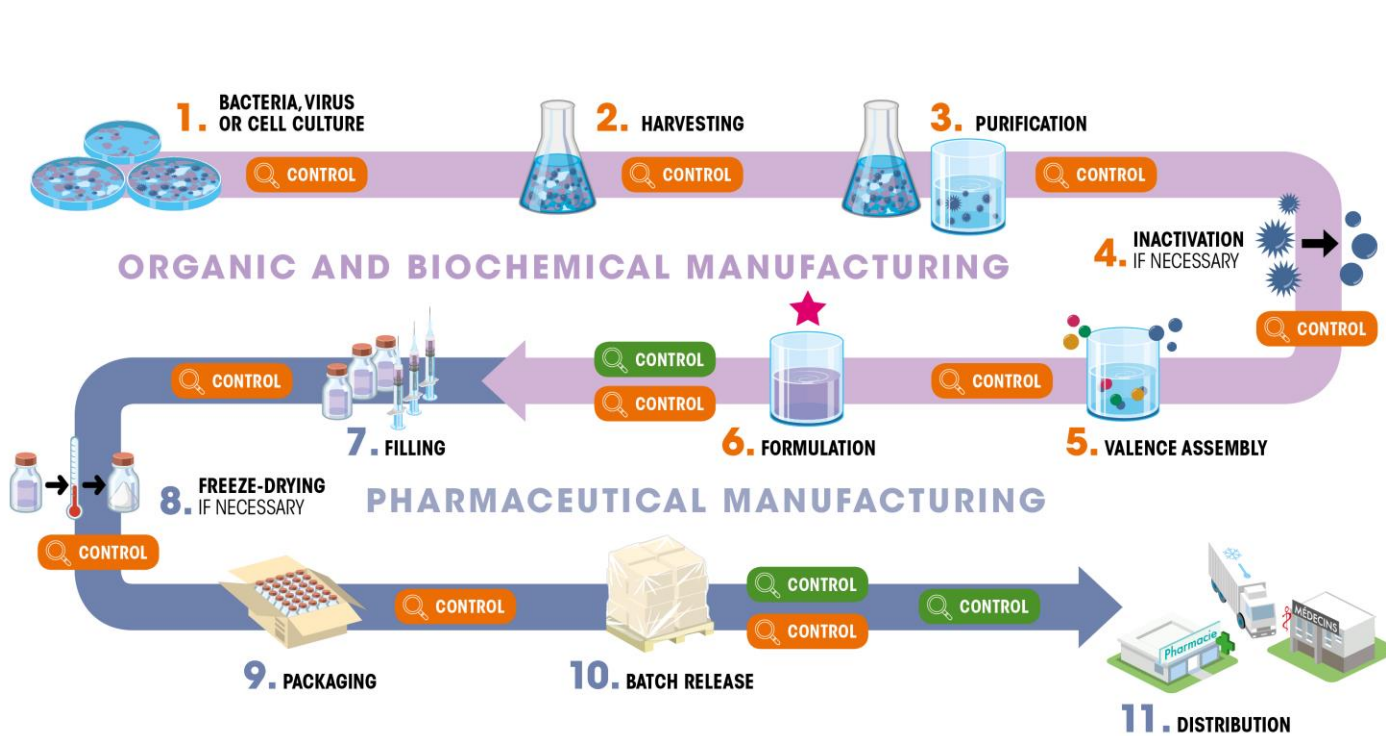
VACCINES
Virus
Bacteria
Recombinant
proteins

- Large molecules, difficult to characterize
- High quality control burden
- Formulation complexity
- Smaller batches, many complex operations
- Viral security constraint (biosafety containment)
- Expensive production



ANTIGEN

VACCINE MANUFACTURING : A LONG WAY!



INTERNAL CONTROL

70% of manufacturing time is dedicated to quality control

from 100 to >1000 quality control for each batch

HEALTH AUTHORITIES CONTROL

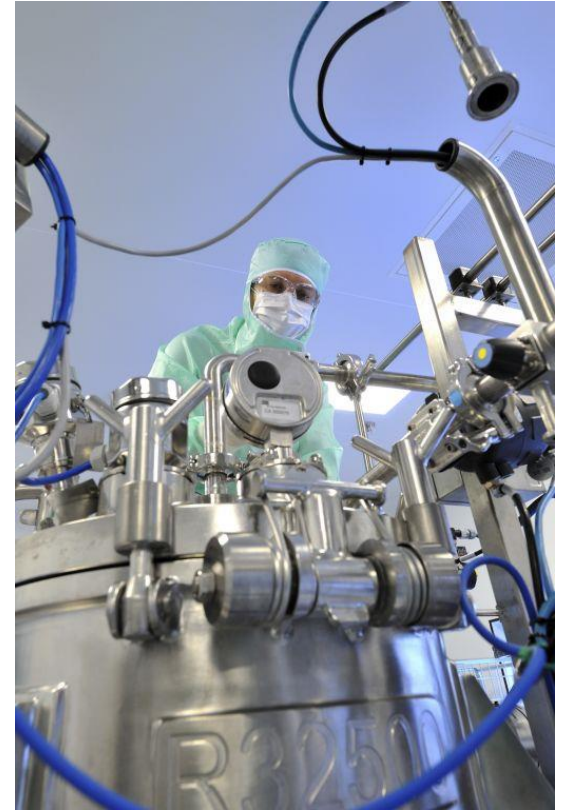
BEGINNING OF THE SHELF-LIFE

Each vaccine contains from 1 up to 9 ANTIGENS

Production takes between 6 and 36 MONTHS

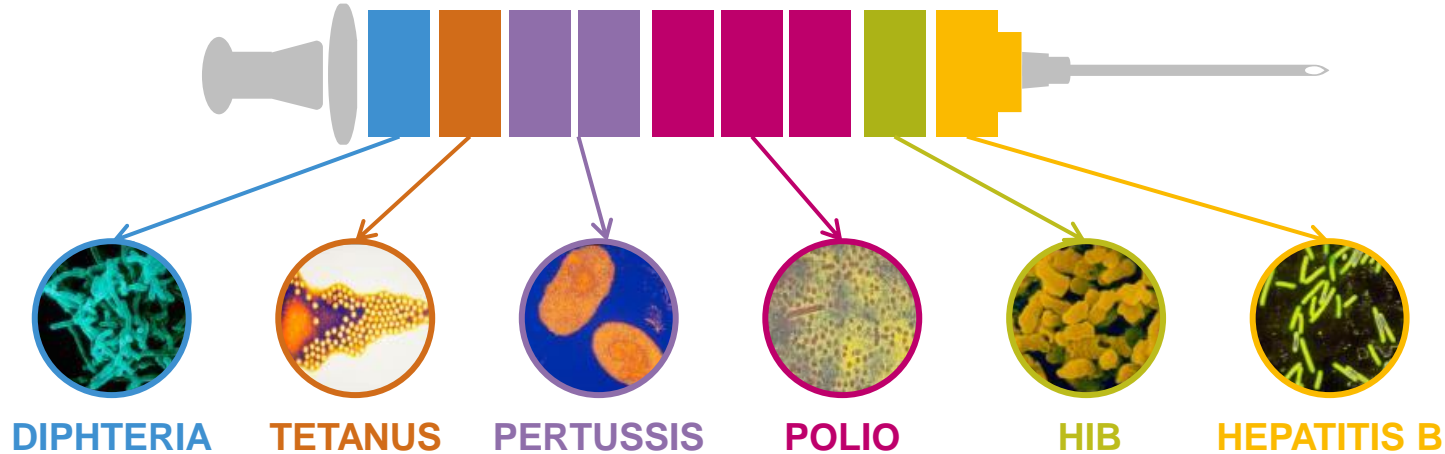
VACCINES, A COMPLEX MANUFACTURING

- High tech / Biotech industry :
Specific know-how to control live micro-organisms
- **Quality oversight all along manufacturing**
 - More than 1000 people in France fully dedicated to Quality
 - Double control by Health Authorities



HEXAVALENT COMBINATION VACCINE

A pediatric combination immunizing against 6 diseases



1 Vaccine

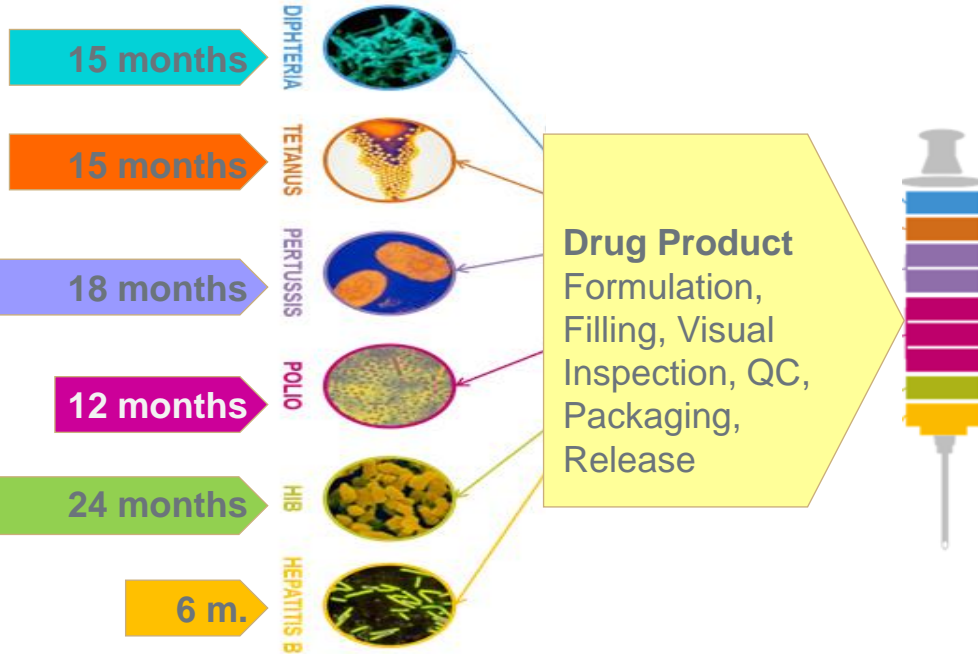
9 Antigens

50 Manufacturing steps

223 Analytical Methods

1277 Individuals tests

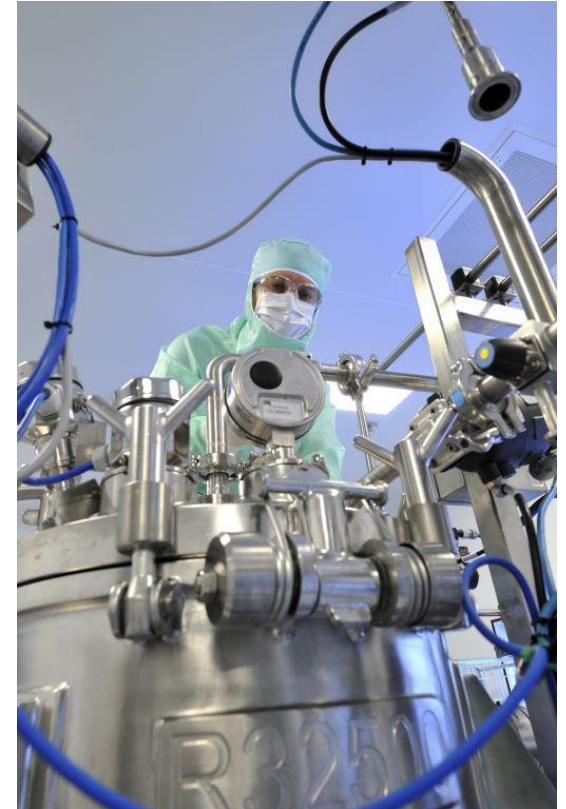
VACCINE BATCH RECORD FIGURES



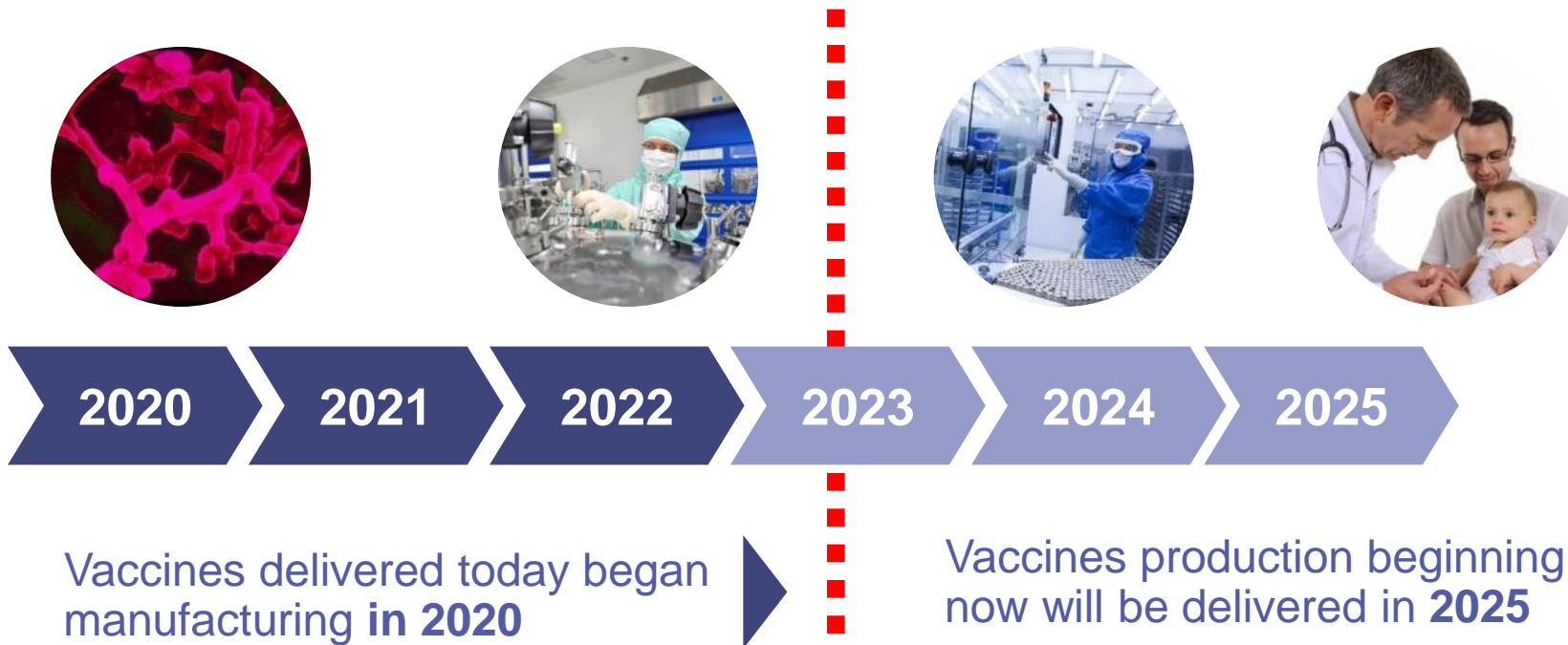
- ~ 1000 pages
- ~ 10 000 data
- > 50 people completing & double checking entries + compliance to limits / specifications

QUALITY POST RELEASE ACTIVITIES

- Stability studies
- Retained sample annual review (US CFR 21)
- Management review for pharmaceutical quality system
- Annual Product reviews
- Periodical Revalidations
- Product Technical Complaints and Pharmacovigilance



MANDATORY ANTICIPATION: Significant time between prod & delivery



3 MAIN CHALLENGES /MANUFACTURING VACCINES

1

COMPLEXITY & LENGTH OF THE PRODUCTION PROCESS

- Biotechnology process
- 7 to 36 months production cycle

2

UNANTICIPATED INCREASE IN GLOBAL DEMAND

- Limited number of vaccine producers worldwide

3

REGULATORY COMPLEXITY

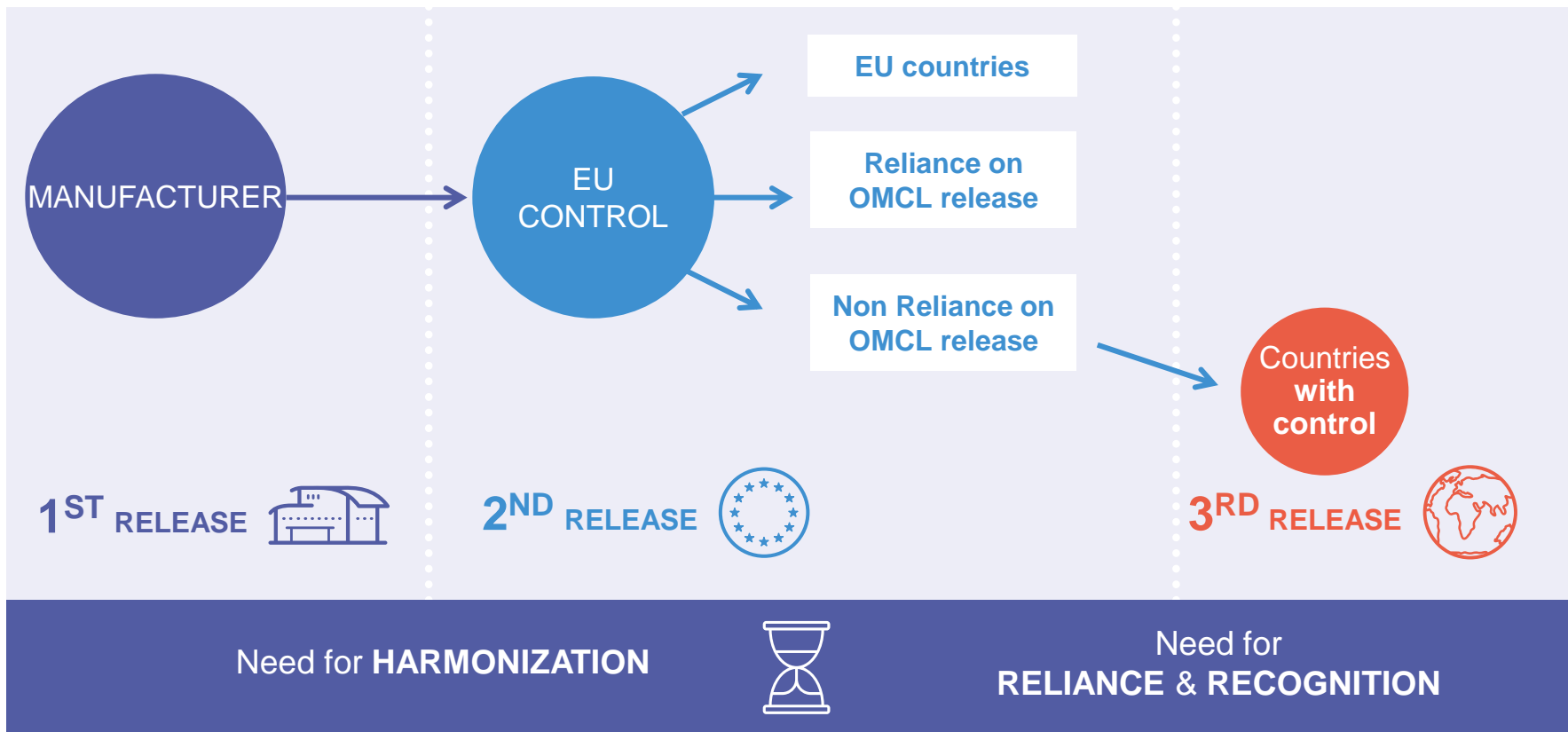
- MULTIPLE REPEAT TESTING Accounts for 70 % of total time for production
- POST APPROVAL CHANGES

**REGULATORY
COMPLEXITY**

**INCREASING
REGULATORY COMPLEXITY**

- HEALTH AUTHORITY BATCH RELEASE
- POST APPROVAL CHANGES

HEALTH AUTHORITY BATCH RELEASE



CHALLENGE OF POST APPROVAL CHANGES

Companies are globalized

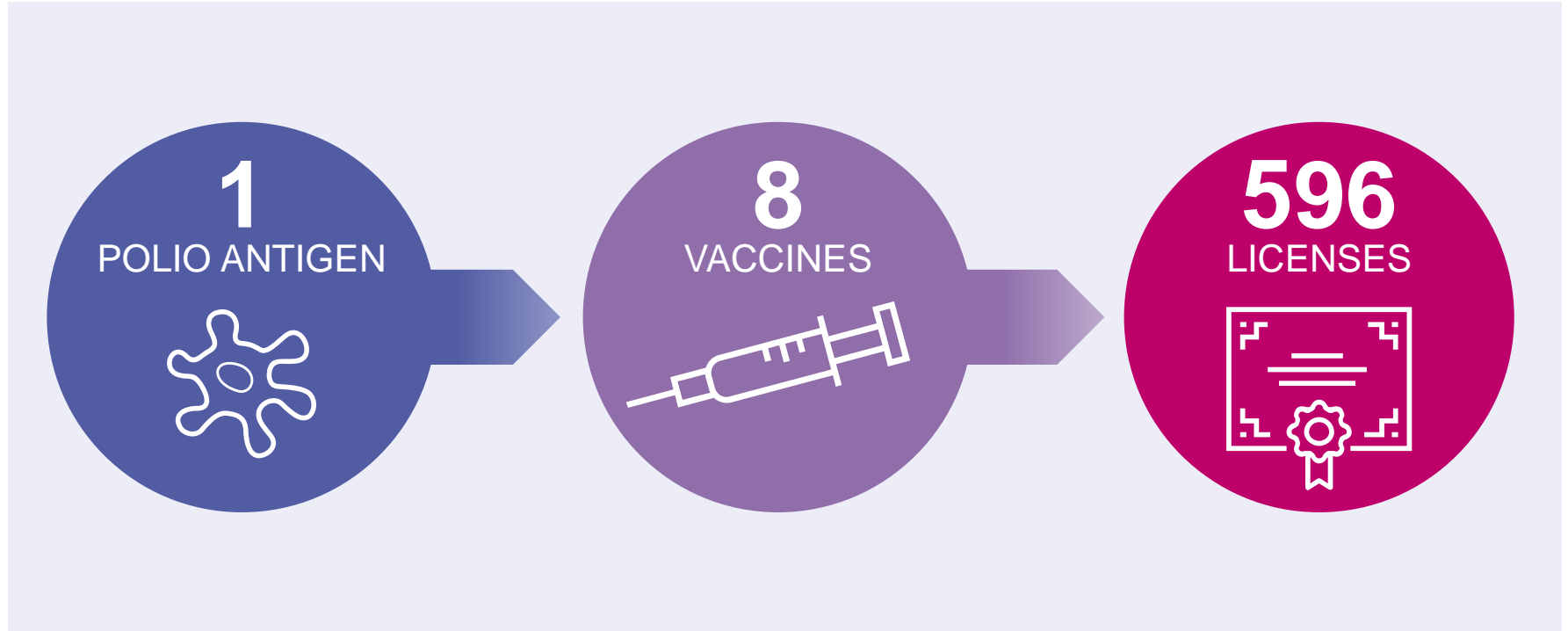


Regulatory approvals are nationalized



1 ANTIGEN, SEVERAL VACCINES, MASSIVE LICENSURES

A tremendous amplification



THE IMPACT OF A SINGLE VARIATION



EXAMPLE
MANUFACTURING
CAPACITY INCREASE
& ASSOCIATED CHANGES

1 VARIATION
FOR
6 CHANGES

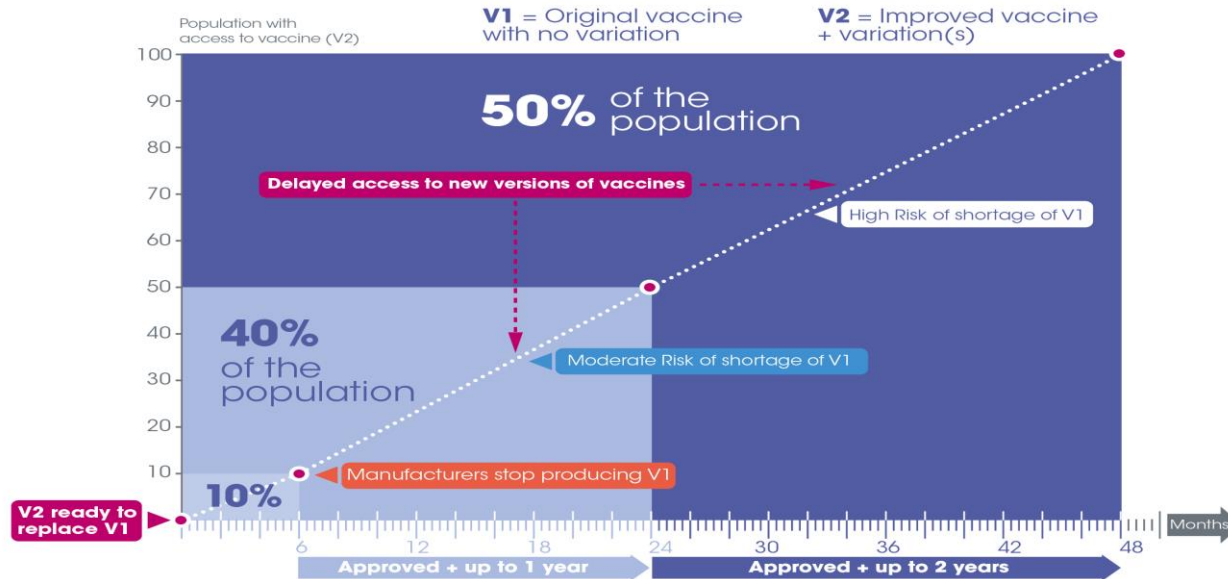


CHALLENGE OF POST APPROVAL CHANGES



1 out of 2 are at risk of shortages due to Post Approval Changes

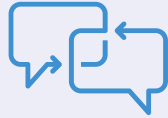
APPROVAL TIMES, RISK OF SHORTAGE AND INEQUITY



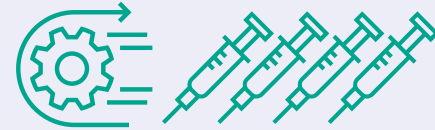
Source: IFPMA

CALL TO ACTION!

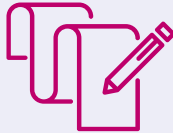
Create an open & continuous dialogue between Public Health Institutions & Industry



Decrease complexity of batch release processes



Reduce post approval changes regulatory burden



Seek common solutions for improved supply



BATCH RELEASE RELIANCE : WHO-NNB



World Health Organization

National Control Laboratory Network for Biologicals

WHO-NCL Network for Biologicals (WHO-NNB)



Optimizing how we work together to accelerate access to quality, safe and efficacious vaccines and other biological products

Globalization of the vaccine industry and the increasing complexity of vaccines requires an international and collaborative approach to regulation

Launched in 2017, WHO-NNB is essential to WHO fulfilling its mandate to safeguard vaccines and facilitate and accelerate access to vaccines. NNB speeds up access to prequalified vaccines through sharing of lot release data of responsible national regulatory authority (NRAs) with recipient country NRAs.

THE NETWORK:

- builds mutual confidence among members
- promotes development of common standards
- facilitates sharing of best practices
- reduces redundant testing; liberating resources for other regulatory activities

"The WHO-NNB has proven to be an invaluable resource for us. By bringing together the national control laboratory community, the network not only facilitates the exchange of critical information and best practices, it has also contributed significantly to the implementation of a reliance approach in our lot release process."

Dr Quinton Meyer (PhD), Director
SA National Control Laboratory for Biological Products

EMERGENCY SITUATIONS - COVID-19

CHALLENGE:
Pandemic response requires an accelerated process if life-saving vaccines are to reach the population quickly. Many manufacturers developed vaccines against COVID-19 in record time. Regulatory processes risk slowing delivery of these vital health products to populations.

SOLUTION:
NNB enables the NRAs of importing countries, with the consent of the manufacturer, to view the NCL lot release data on the NNB SharePoint. Through this transparency and access to quality information an importing country can confidently rely on testing already undertaken.

BENEFIT:
Transparency around vaccine quality is enhanced, and trust is promoted between manufacturers and regulators. This saves financial resources and, most importantly, shortens the time taken to make the vaccine available for administration.

WORKING TOWARDS A FUTURE WHERE LIFE-SAVING VACCINES ARE AVAILABLE FOR EVERYONE EVERYWHERE



PROMOTING GLOBAL COLLABORATION AND RELIANCE

► Information Exchange

Serving as a platform for confidential information exchange of quality and technical information on vaccines (and other biological medicinal products) prequalified by WHO.

► Improving Procedures

Encouraging reliance on the batch release of the respective Network members by recipient countries and contributing to more cost-effective testing and more effective regulatory oversight.

► Forging Relationships

Cooperation and networking are increasing regulatory efficiency through greater reliance on existing quality resources, data and existing expertise.

► Sharing Best Practices

Promoting development of harmonized common standards and best practice, including the use of the 3R principles: reduction, replacement, refinement of animal based testing.

HOW CAN YOU PARTICIPATE

FULL MEMBERSHIP

- National regulatory authorities (NRAs)/national control laboratories (NCLs) from countries producing WHO-prequalified vaccines (or other biological medicinal products) who have responsibility for release of those vaccines
- WHO-contracted NCLs that perform physical testing of vaccines for WHO

ASSOCIATE MEMBERSHIP



World Health Organization

CONCLUSION

- Reducing complexity brings **PUBLIC HEALTH BENEFITS**
 - Enhanced innovation
 - Fewer shortages, shorter time to market
 - More sustainable vaccine supply contributing to higher coverage rates & population protection
- Vaccination is a global need = needs a global approach
- Early cooperation between parties and anticipation are key

THANK YOU