COMPLEXITY OF QUALITY CONTROL AND VACCINES MANUFACTURING

VACCINES PRODUCTION: HIGHLY COMPLEX

Increasing complexity, controls and cost to produce

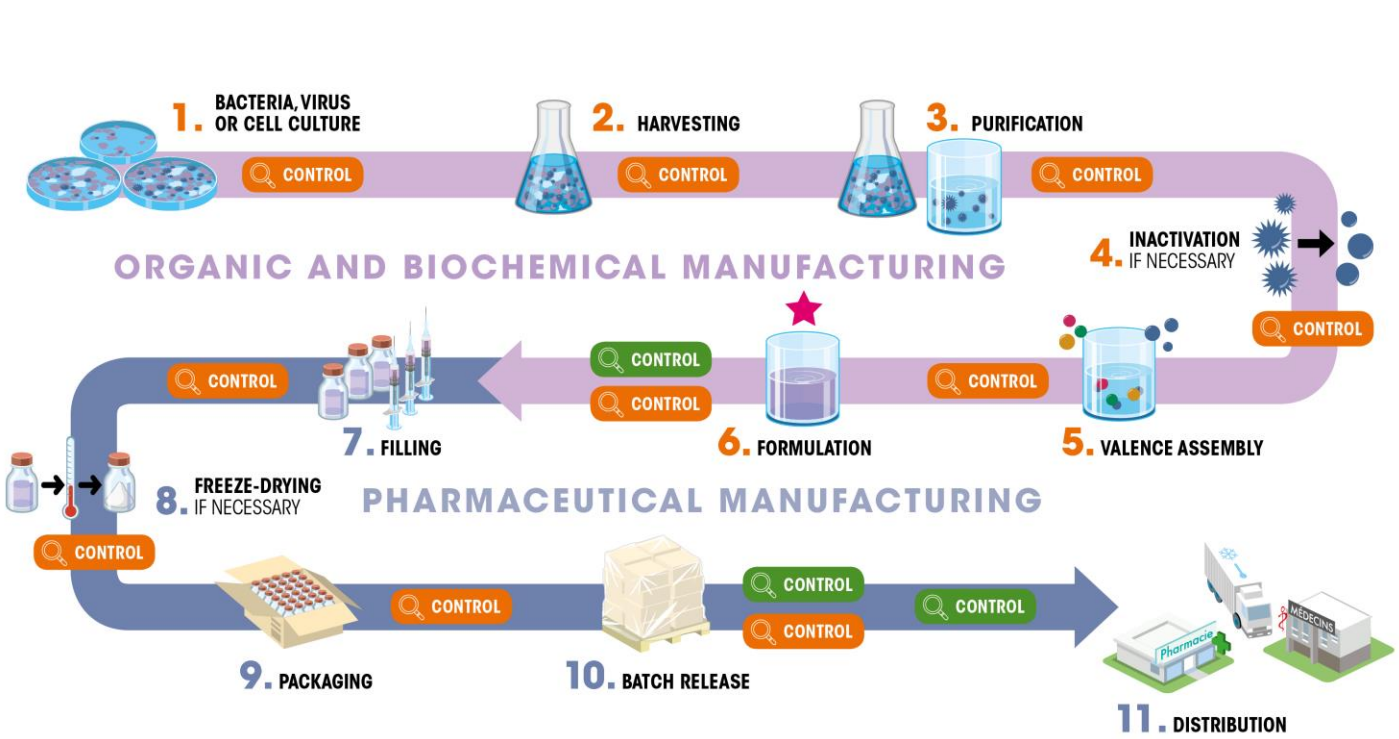
SMALL MOLECULE DRUGS

- **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**

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

BEGINING OF THE SHELF-LIFE

Each vaccine contains form **1** up to **9 ANTIGENS**

Production takes between **6** and **36 MONTHS**

VACCINES, A COMPLEX MANUFACTURING

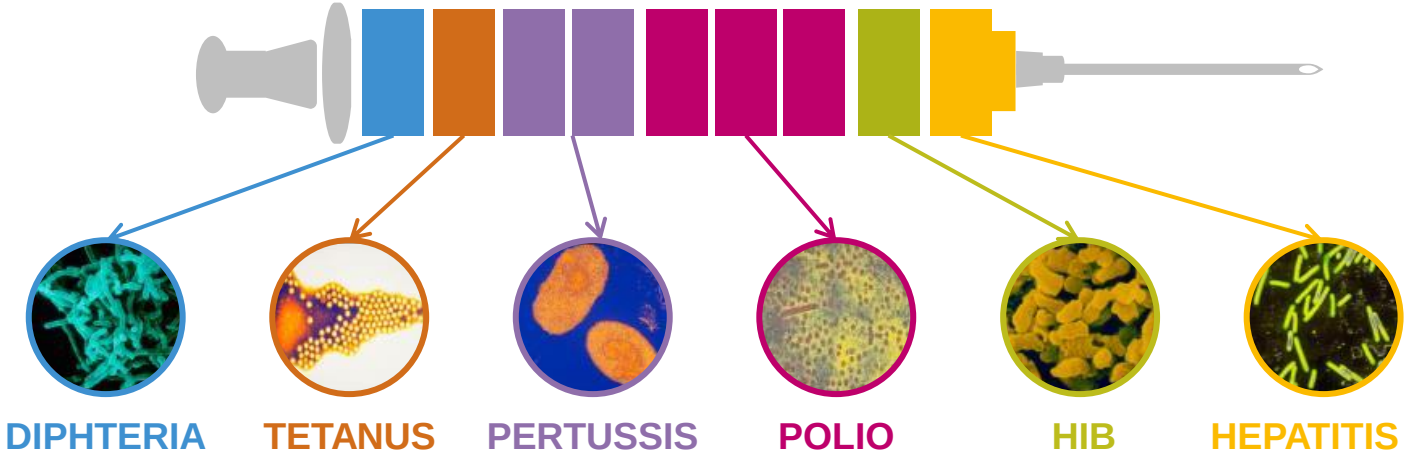
- High tech / Biotech industry **:**

  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**

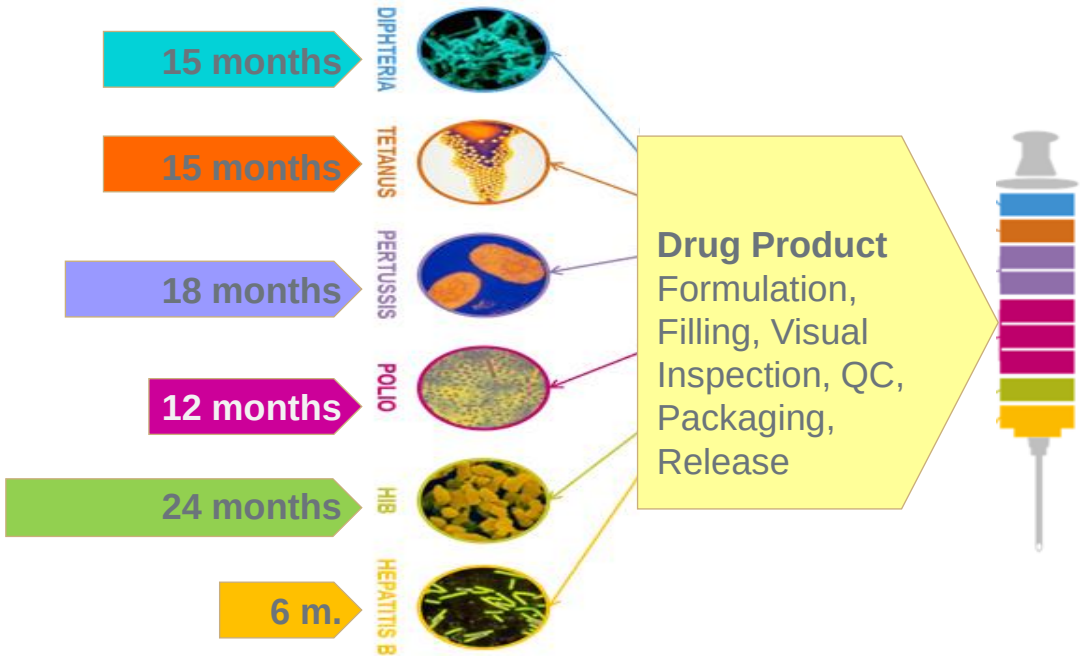
HEXAVALENT COMBINATION VACCINE

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

2020 | 2021 | 2022 | 2023 | 2024 | 2025

Vaccines delivered today began manufacturing **in 2020**

Vaccines production beginning now will be delivered in **2025**

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

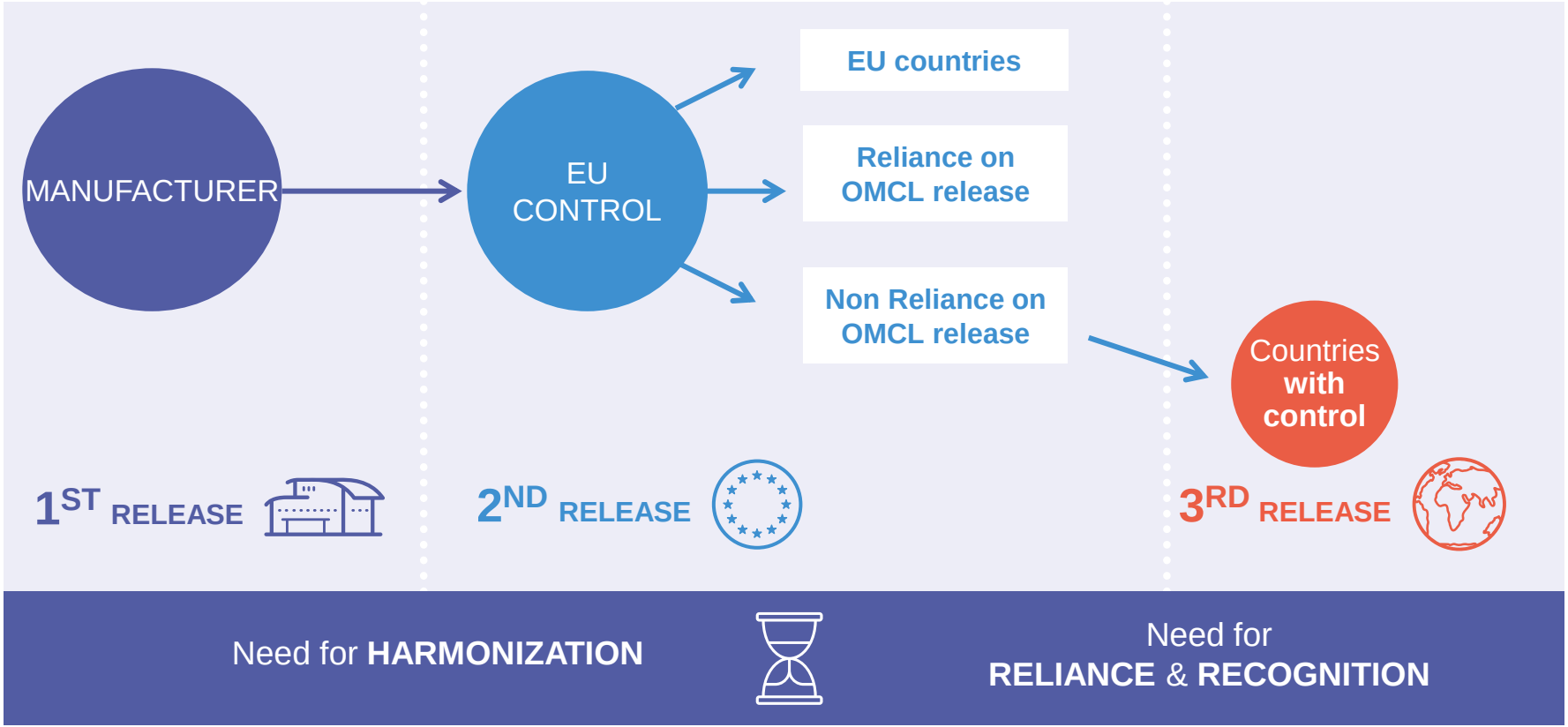
REGULATORY COMPLEXITY

INCREASING
REGULATORY COMPLEXITY

- HEALTH AUTHORITY BATCH RELEASE
- POST APPROVAL CHANGES

REGULATORY COMPLEXITY

HEALTH AUTHORITY BATCH RELEASE



REGULATORY COMPLEXITY

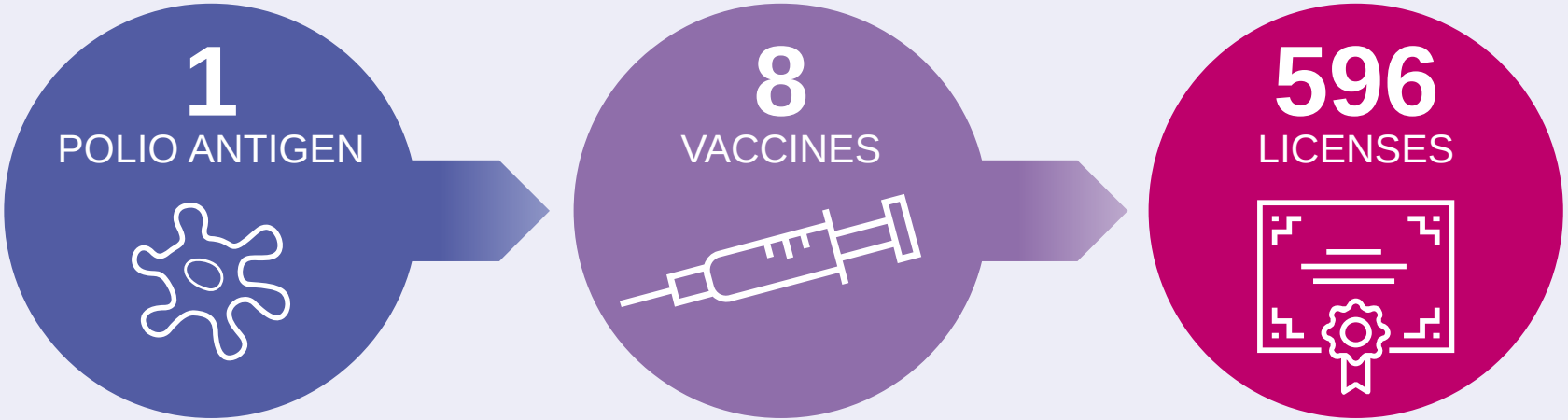
CHALLENGE OF POST APPROVAL CHANGES

Companies are globalized

Regulatory approvals are nationalized

1 ANTIGEN, SEVERAL VACCINES, MASSIVE LICENSURES

A tremendeous amplification



THE IMPACT OF A SINGLE VARIATION

EXAMPLE

MANUFACTURING CAPACITY INCREASE & ASSOCIATED CHANGES

1 VARIATION FOR 6 CHANGES

7 Products licensed in 138 countries

Major reporting level **62** countries

Minor reporting level **37** countries

No reporting **39** countries

22 countries raised

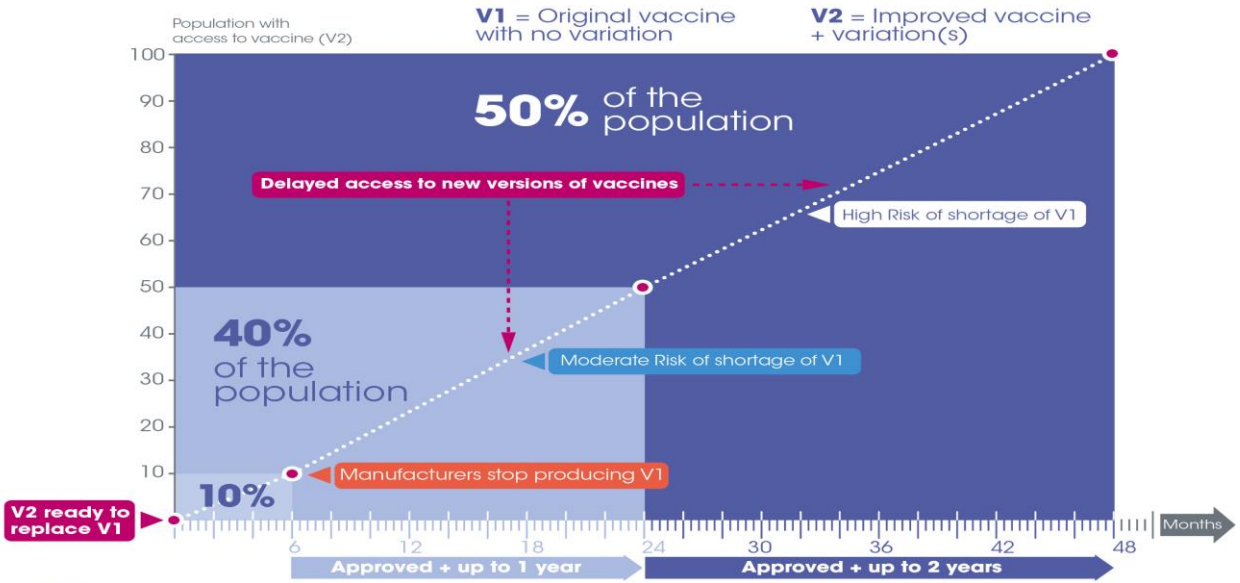
177 questions of which only

19 are different

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

PROMOTING GLOBAL COLLABORATION AND RELIANCE

►Information Exchange

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

►Forging Relationships

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

►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.

►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

sanofi

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