Strengthening Vaccine Manufacturing and Regulation in Africa

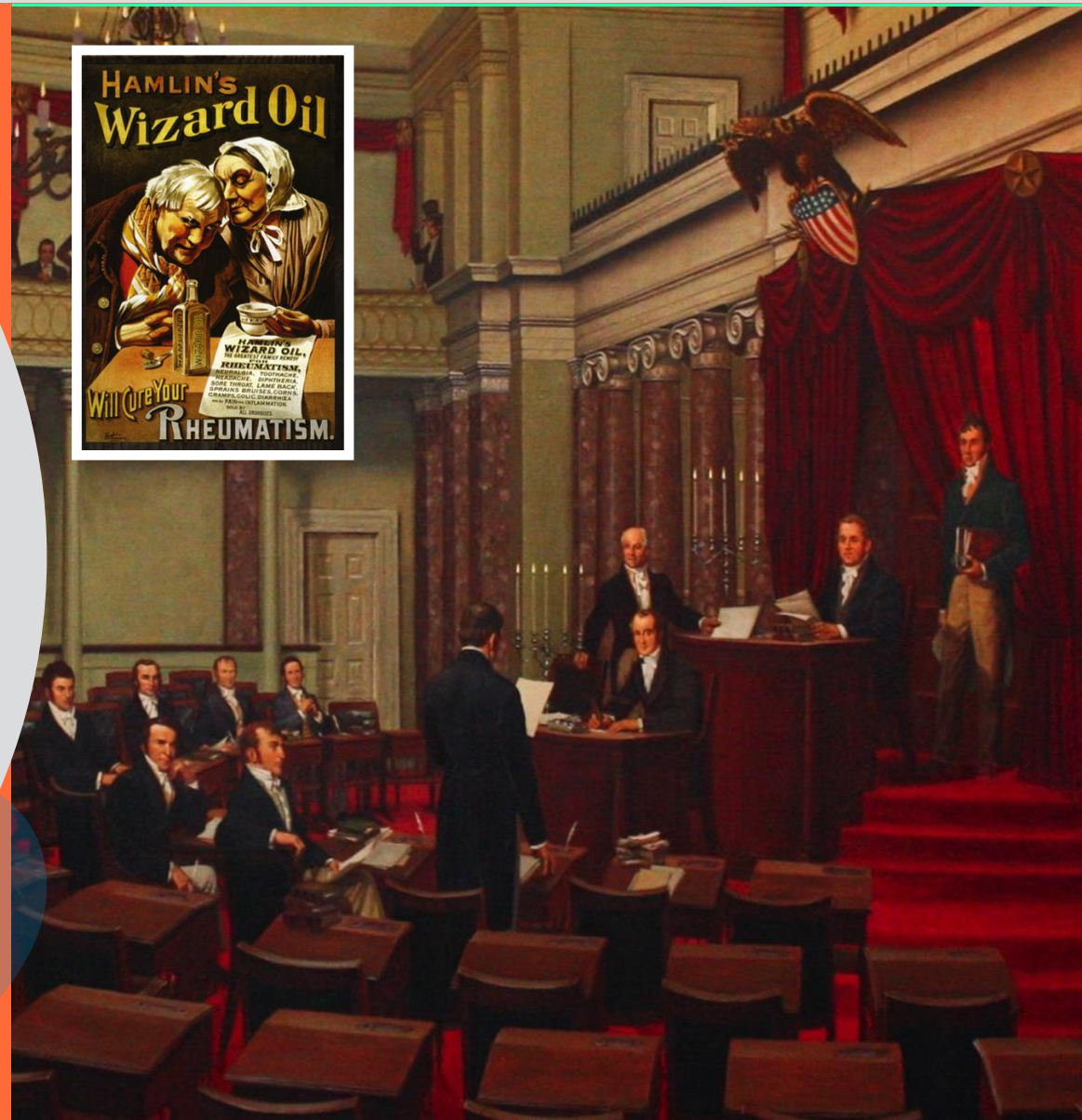
Jude Nwokike
Vice President USP, PQM+ Program Director

October 19, 2022

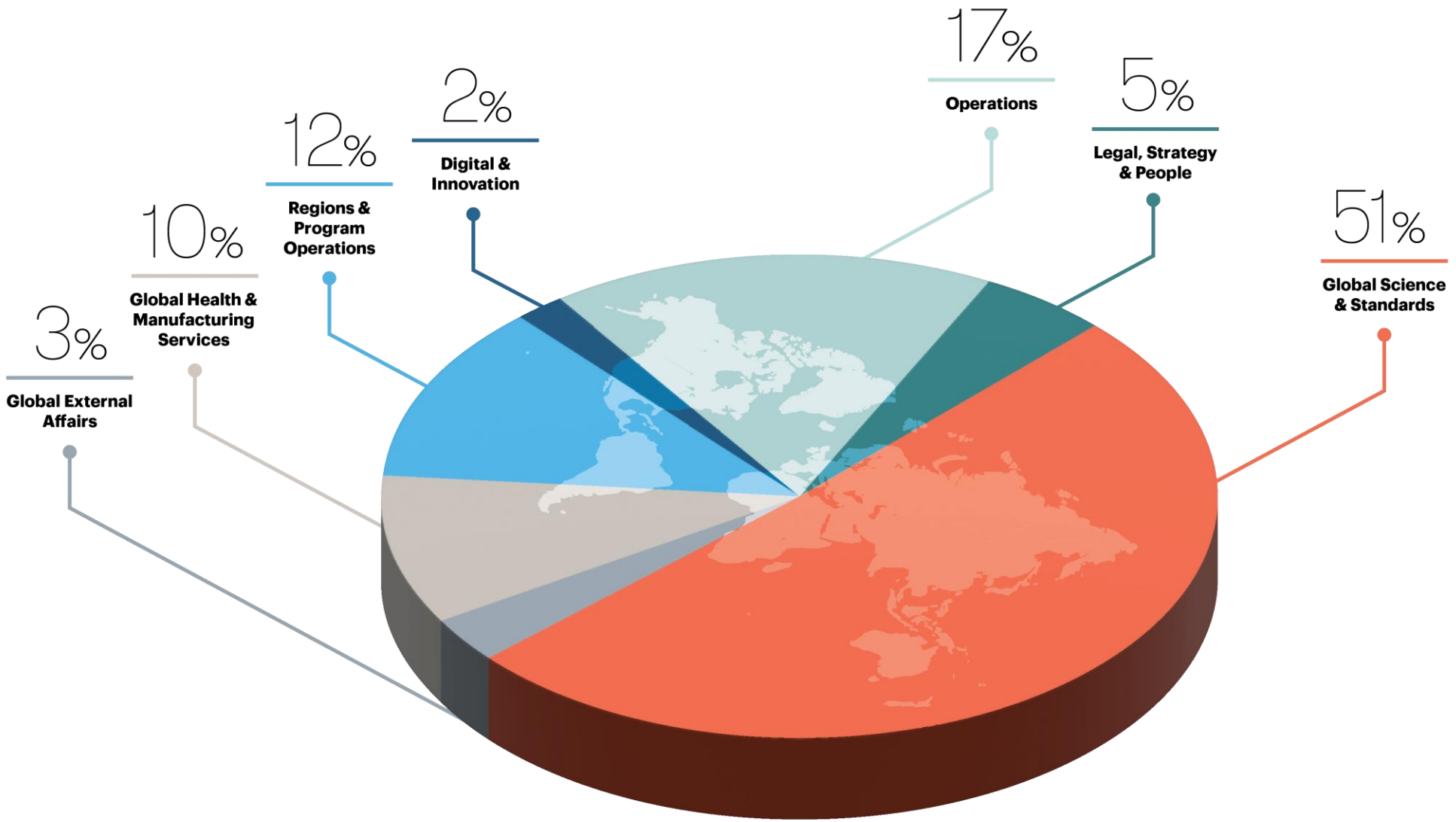
200 usp
The standard of trust

Our enduring mission

To improve global health through public standards and related programs that help ensure the quality, safety, and benefit of medicines and foods.



More than 1300 USP staff deliver our global mission



Our impact on global health systems

In the last 30 years, USP's efforts improved regulations, laboratories, medicines safety, and health system stewardship

50+

Programs in 50+ countries across 4 continents implemented by USP

100+

100+ manufacturers engaged with **41** products achieving WHO PQ or SRA approvals

90+

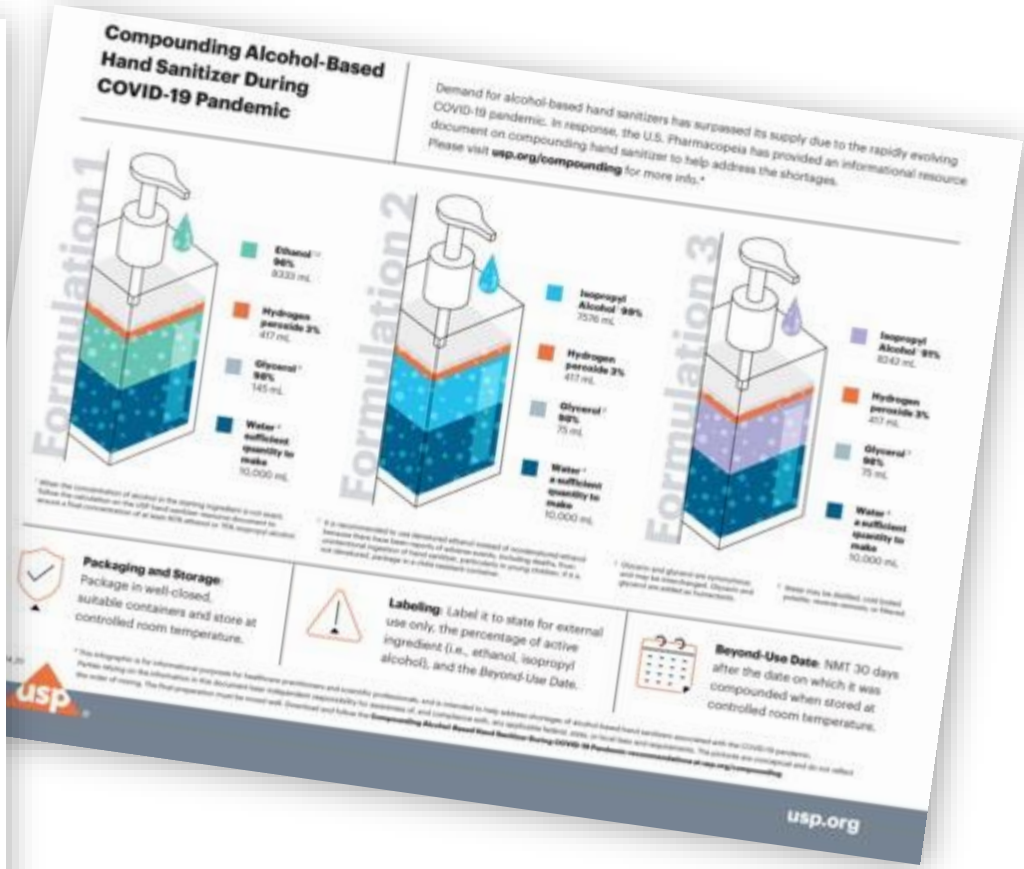
90+ labs trained in global standards and best practices;
25+ ISO accredited,
21+ WHO PQed

Public health priorities we are helping to address

- COVID-19 response
- Supply chain resiliency
- Harnessing advances in biomedical science
- Expanding regulator capacity

COVID-19 response

Helping to ensure the supply of quality vaccines, treatments and health information



Shared vision

PQM+ is a cooperative agreement between USAID and USP to sustainably strengthen medical product quality assurance systems in low- and middle-income countries.

USAID FROM THE AMERICAN PEOPLE + USP

Initiatives to Strengthen Vaccine Manufacturing and Regulation in Africa

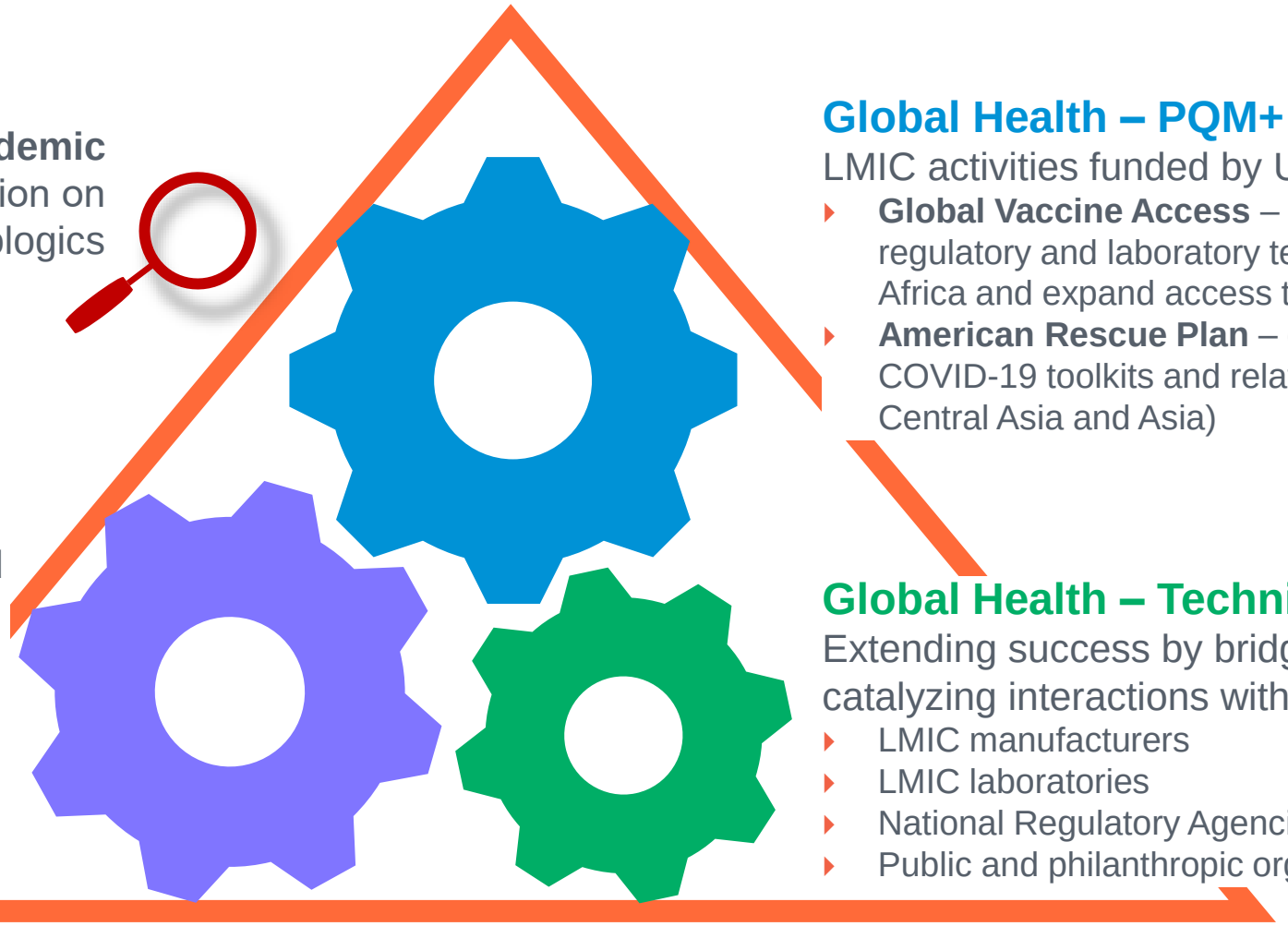
Zlatka Kostova Lenard, PhD

PQM+ Vaccines Director

Our vaccines ecosystem

- **An integrated approach to global health solutions**

SARS-CoV-2 Pandemic
Refocused USP's attention on quality of vaccines and biologics



Global Biologics

Best practices and analytical procedures for manufacture and quality testing

- Standards, compendial tests, USP- NF general chapters
- Handling & Assessment toolkits
  Substandard strategies
  Hand sanitizer compounding
- Vaccine courses

Global Health – PQM+

LMIC activities funded by USAID

- **Global Vaccine Access** – strengthening regulatory and laboratory testing capacity in Africa and expand access to COVID-19 vaccines
- **American Rescue Plan** – dissemination of USP COVID-19 toolkits and related training (Africa, Central Asia and Asia)

Global Health – Technical Programs

Extending success by bridging gaps and catalyzing interactions with

- LMIC manufacturers
- LMIC laboratories
- National Regulatory Agencies
- Public and philanthropic organizations

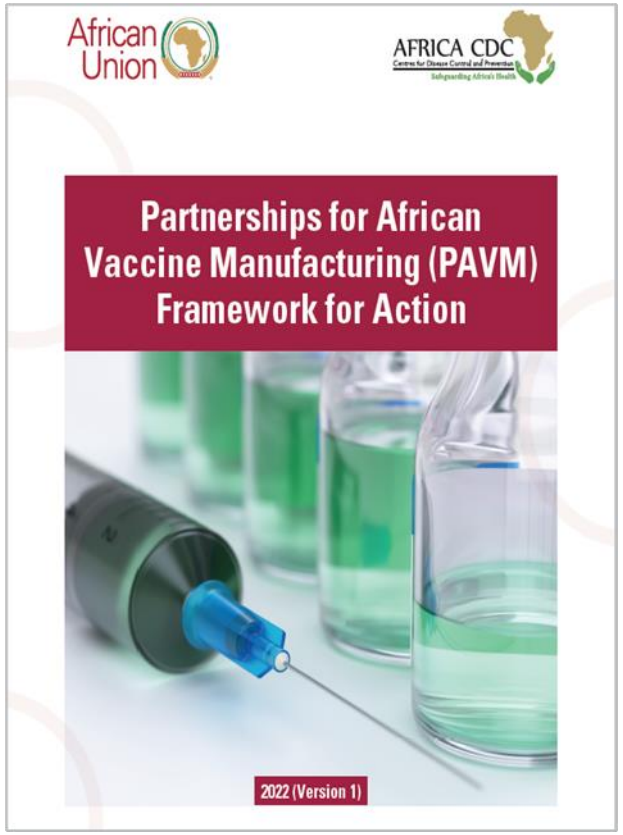
Science led approach to technical assistance

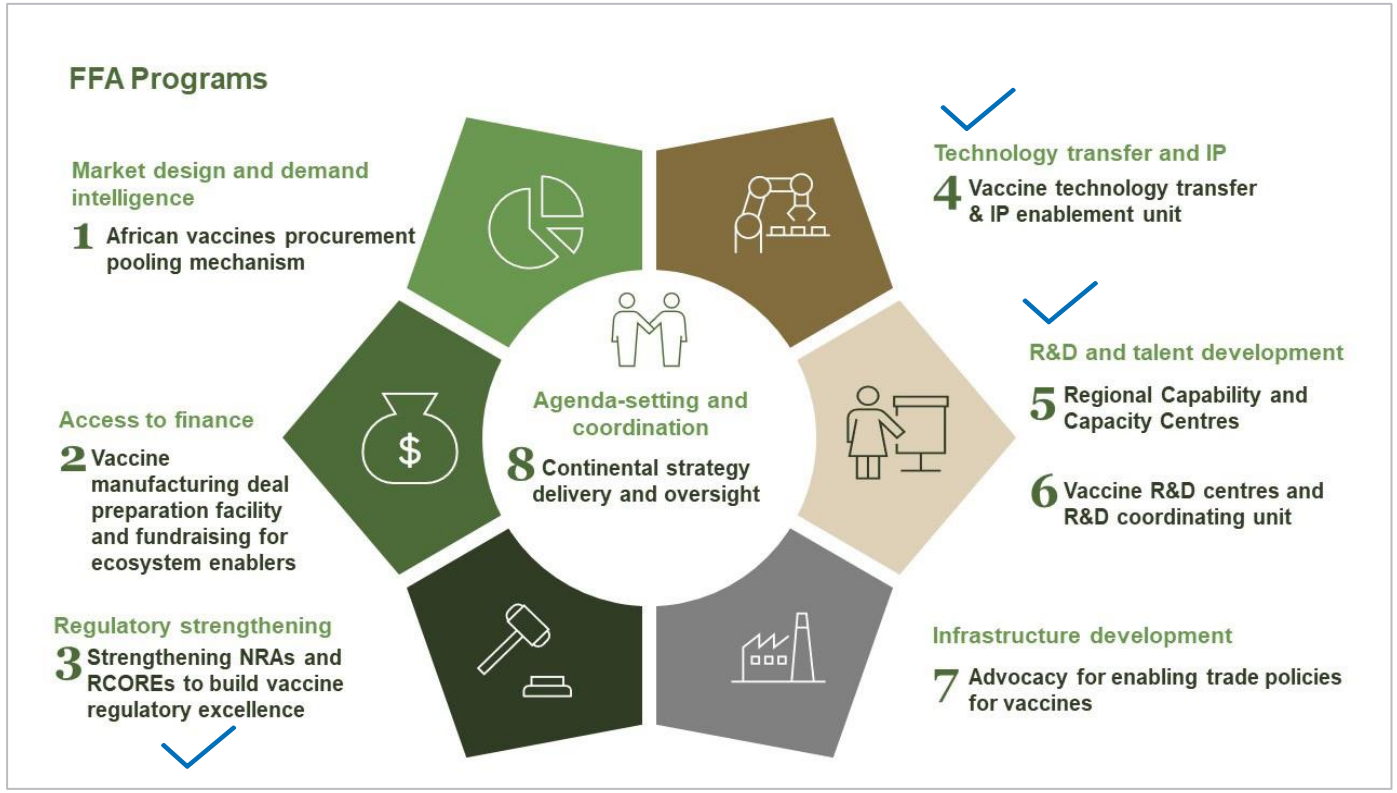
- Bridging needs and solutions through understanding of the challenges
- Catalyzing implementation based on knowledge of LMIC gaps

- Infectious Disease
  - HIV, TB, malaria
  - NTD
  - Under recognized high disease burden
  - Epidemic/pandemic
- Antimicrobial stewardship / AMR
- Education & thought leadership
  - Product complexity (DS, DP)
  - Technologies (platforms and adjuvants)
  - Development and life-cycle strategies (improvements, combinations, multi-target)
- Manufacturing
  - Facilities and processes
  - Primary, secondary, distribution
  - Product dossier and PV
- Laboratories
  - NCL (accreditation, testing and lot release)
  - Clinical diagnostics
  - (Microbiology, clinical serology)
- Regulatory systems
  - Dossier review
  - Inspections, market authorization
  - PV, RB-PMS

AU goal to meet 60% of Africa's vaccine demand by *local* manufacturing by 2040

- USP/PQM+ activities directly support PAVM's vaccine manufacturing objectives

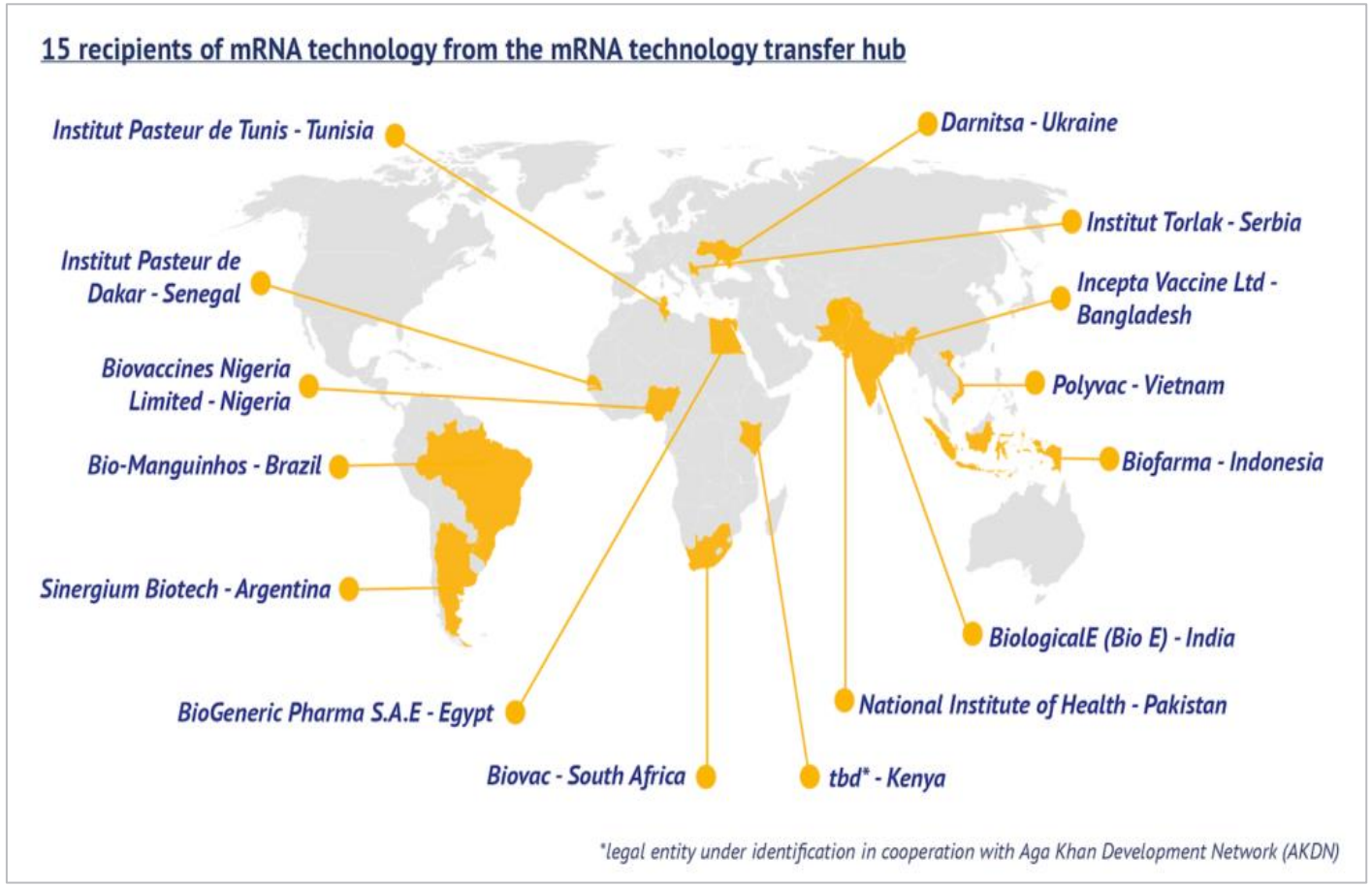




USP/PQM+ Leverages Ongoing Global Initiatives

mRNA Technology Transfer Hub Programme

African Union · AFRICA CDC · Afrigen Biologics & Vaccines · BIOVAC · saMRC · medicines patent pool · World Health Organization



U.S. Government's Initiative for Global Vaccine Access – Global VAX

- Initiative to accelerate U.S. vaccine delivery assistance around the World[1]
  - Boost local vaccine manufacturing by supporting LMICs poised to produce vaccines, build regulatory capacity, transfer "know-how" to emerging manufacturers, and provide strategic planning and other assistance
  - Complements US International Development Finance Corporation's investments to scale regional manufacturing of COVID-19 vaccines
- PQM+ engaged to provide technical assistance to six African countries: Ghana, Kenya, Nigeria, Rwanda, Senegal, and South Africa
  - Build regulatory and quality control laboratory capacity
  - Support the nascent vaccine manufacturing industry in Africa
  - Provide strategic planning assistance

[1] https://www.usaid.gov/sites/default/files/documents/Global_VAX_Factsheet_Update_May_2022_FINAL_FOR_UPLOAD3.pdf

Vaccine Manufacturing Workshop – Objectives

- The objectives of this joint activity are to:
  - Develop the vaccine manufacturing competency of various stakeholders, including African NMRAs, academics, and the vaccine manufacturing industry
  - Provide a forum of engagement and networking for NMRAs, vaccine manufacturers, and international stakeholders
  - Advance the objectives of the WHO-supported mRNA Technology Transfer Hub and Spokes arrangement
  - Contribute to the PAVM 2040 target of adding 10,500 new full-time equivalents to the vaccine workforce across the African continent and help address the talent gaps identified by the RCCC

High Level Workshop Agenda

This joint activity will consist of a workshop centered on vaccine manufacturing and in-person visits to South African vaccine manufacturing facilities (Biovac and Afrigen). The workshop will be organized around three focus areas.

Overview of Vaccine Development and Manufacturing	• SME presentations on the fundamentals of vaccine product development and GMP manufacturing, with emphasis on mRNA and viral vector vaccines • *Goal is to lay a solid foundation to build on by giving participants a complete view of the complexity and nuances of vaccine manufacturing*
Case Studies	• Real-life case study presentations by workshop participants for interactive brainstorming and problem-solving • *Goal is to provide an informal forum for engagement between the NMRAs, vaccine manufacturers and other stakeholders leading to a better understanding of common needs and challenges and to the design of sustainable interventions*
Networking	• Discussion and review of Biomanufacturing Competency Framework and Database • Formation of an African Community of Practice • Compendium of training materials to take home • *Goal is to facilitate the establishment of collaborative and sustainable working relations among the participants*

Global VAX | Vaccine Manufacturing Workshop

BUILDING A SUSTAINABLE & COMPETENT AFRICAN WORKFORCE

Promoting the Quality of Medicines Plus Program (PQM+)

USAID FROM THE AMERICAN PEOPLE

usp

December 6 – 9, 2022

Century City Conference Centre
Cape Town, South Africa

Register: *https://cvent.me/g3MmxN*

LIVESTREAM AVAILABLE

Convened by the USAID-funded and USP-led Promoting the Quality of Medicines Plus (PQM+) program in collaboration with the African Union Development Agency New Partnership for African Development (AUDA-NEPAD), this workshop aims to enhance the understanding of practical aspects of vaccine development, manufacturing complexities, regulatory dossier compilation and stakeholder engagement. This aims to contribute to the PAVM 2040 target of developing the vaccine manufacturing competency in Africa , and advance the objectives of the WHO-supported COVID mRNA Technology Transfer Hub and Spokes arrangement.

Product Supply Management – Chemistry Manufacturing Controls / Regulatory Systems Strengthening

Frederick Meadows, PhD

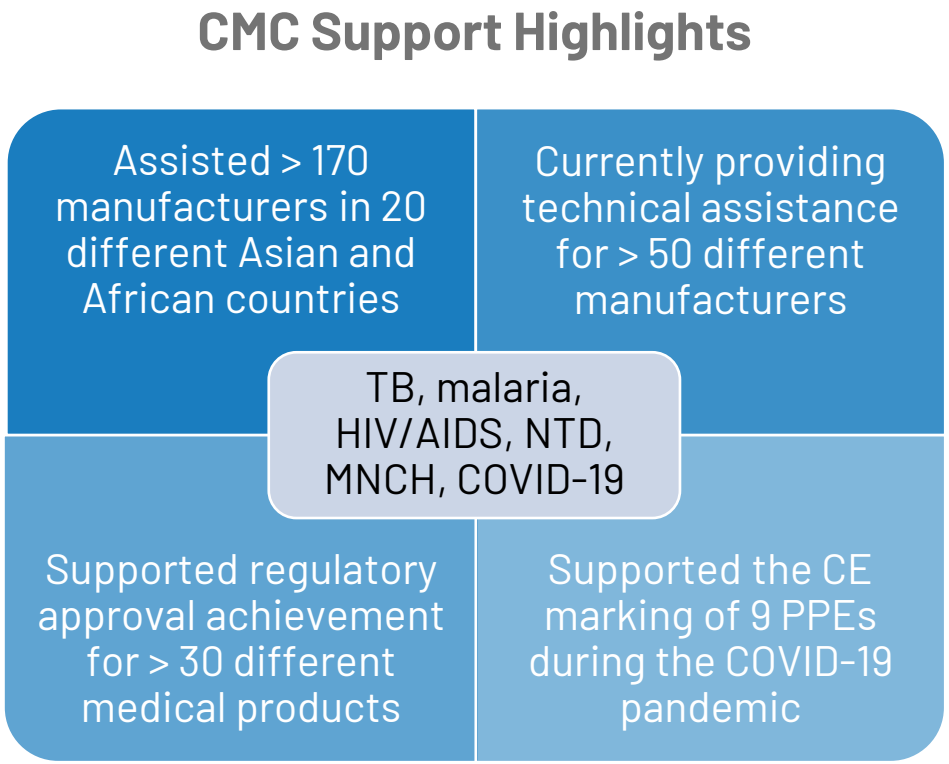
Senior Technical Advisor

USP's Technical Support Areas

- PQM+ provides technical assistance to low- and middle-income countries (LMICs) under the following areas:
  - Regulatory Systems Strengthening (RSS)
  - Laboratory System Strengthening (LSS)
  - Product Supply Management and Chemistry, Manufacturing, and Controls (CMC)
  - Workforce Development
  - Pharmaceutical Sector Strategy and Planning

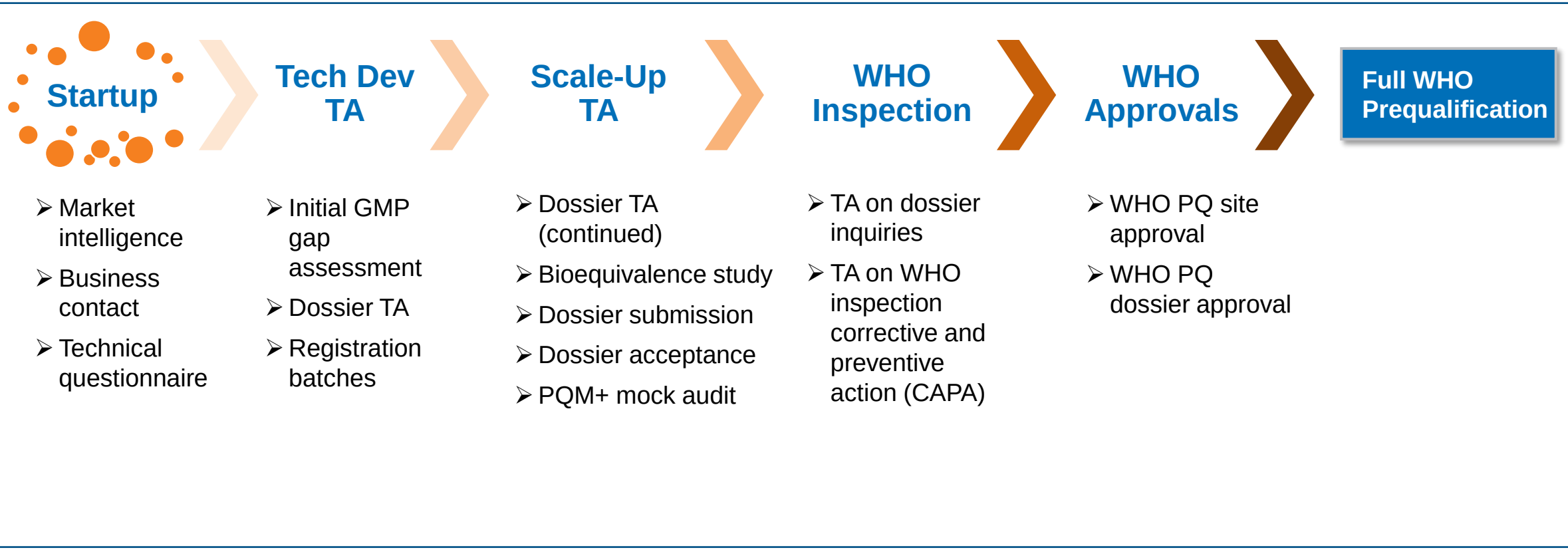
CMC – Global Support to Pharmaceutical Manufacturers

- USP/PQM+ provides CMC technical assistance to manufacturers across the world to ensure product quality, efficacy and safety, and compliance with international QMS & GMP standards
- The objective is to increase the supply of quality-assured essential medical products of public health importance



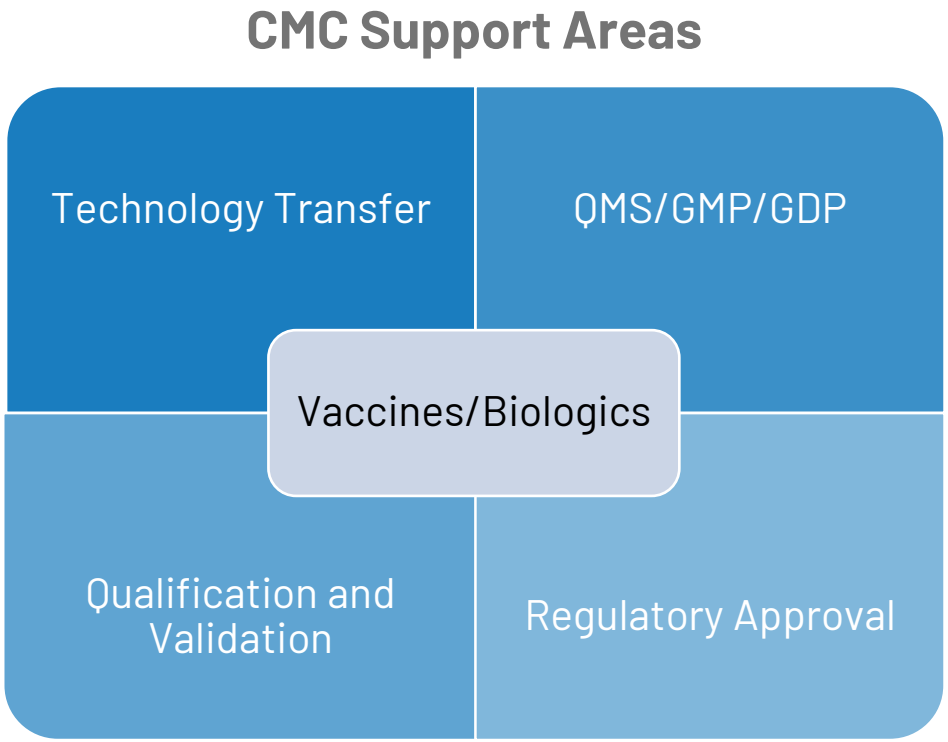
The CMC Team Supports Manufacturers toward WHO PQ

- The WHO PQ procedure is a multistep process
  - Timelines depend on manufacturer's commitment and available resources



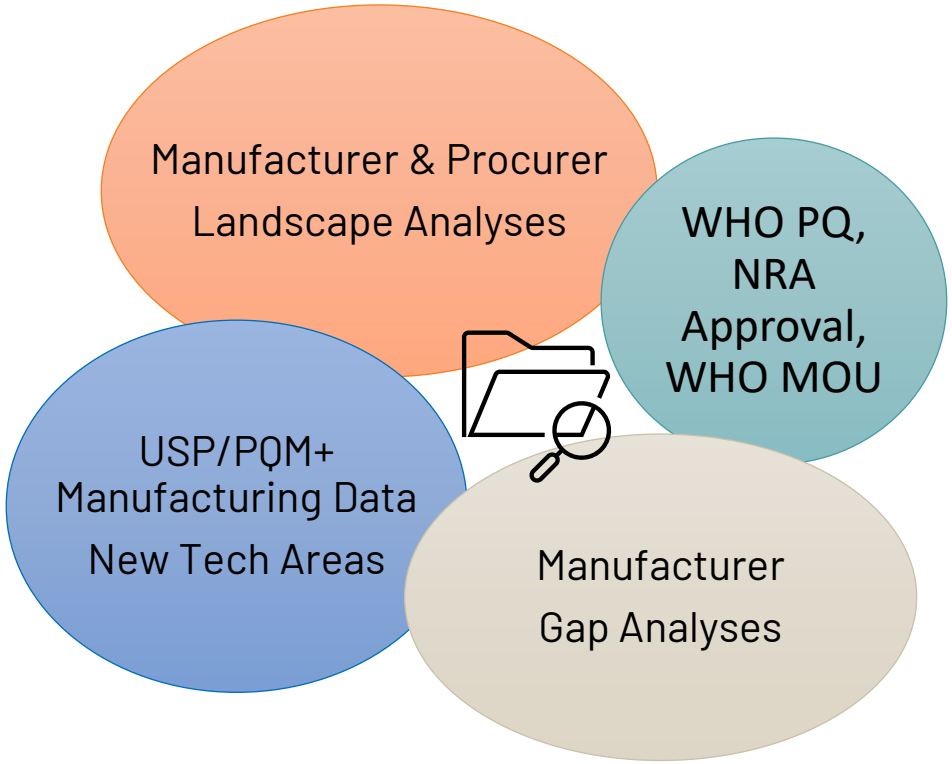
CMC – Global Support to Vaccine Manufacturers

- USP/PQM+ has the technical expertise to support the growth of local vaccine manufacturing capacity in Africa by providing technical assistance in:
  - CMC gap analysis and mitigation strategies to ensure product quality, efficacy and safety, and compliance with international QMS & GMP standards
  - Technology transfer for biological drug substance (DS) and/or drug product (DP) processes from an originator/donor to a recipient site
  - Qualification and validation of DS/DP manufacturing facilities to ensure compliance with international standards.
  - Achievement of regulatory approval for locally manufactured vaccines



CMC – Model of Continuous Improvement

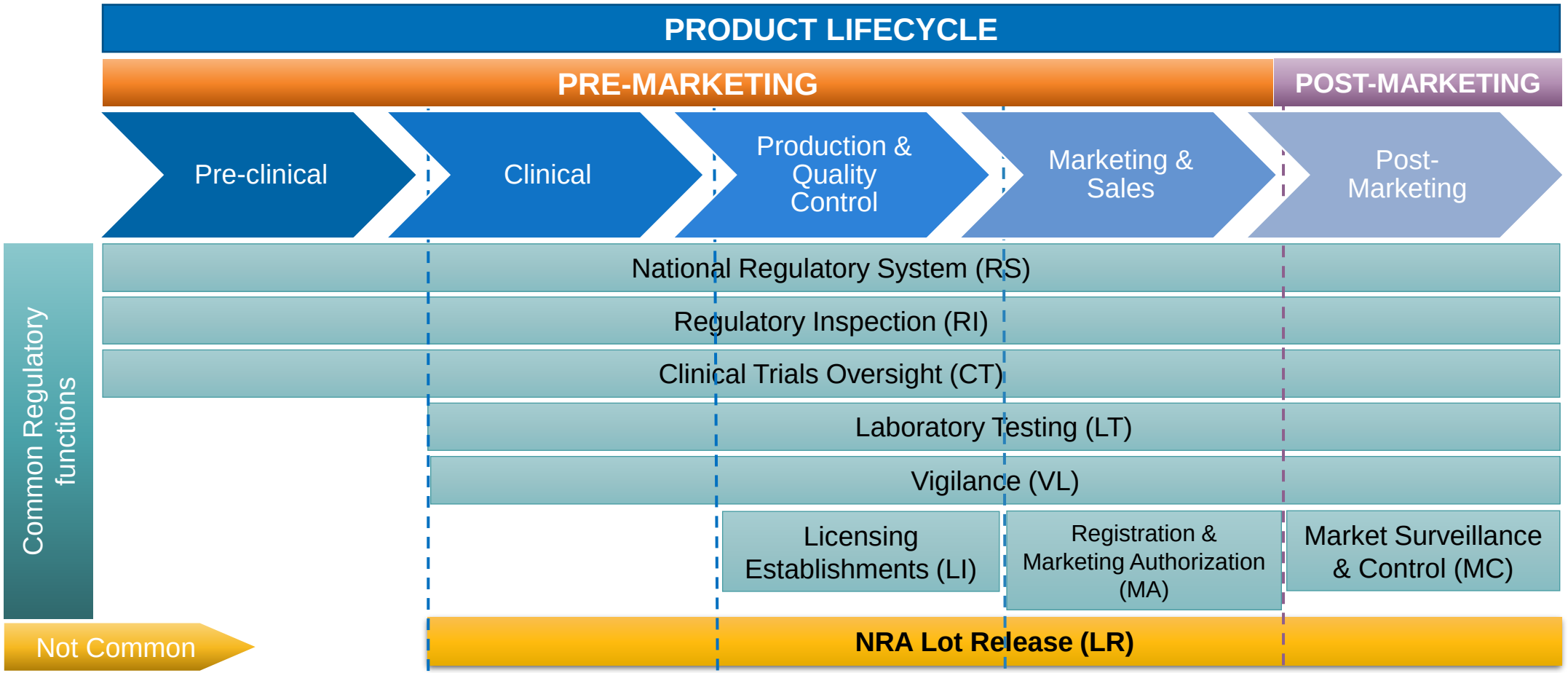
- The CMC team analyzes data obtained from diverse activities to deliver new and improved technical assistance and sustainable results



- Develop Improved Interventions for Sustainable Results
- Generate Next Generation Tools:
  - Risk-Based GMP Inspection
  - Remote Inspection
- Introduce New Areas of Support:
  - Vaccines
  - Advanced Manufacturing Technologies

RSS – Regulatory Functions & Product Lifecycle

- USP/PQM+ support to NMRAs in line with WHO GBT Regulatory Functions covers all the Product Lifecycle stages



Adapted from A. Khadem and M. Refaat - WHO RSS program and Overview of the WHO GBT

Regulatory compliance: NMRA Lot Release Program

- **Lot Release Process:**
  1. The manufacturers' summary protocol should be reviewed by an NRA/NCL before release of a vaccine lot onto the market
  2. Product consistency should be assessed through trend analysis on successive lots.
  3. Where NCLs do not receive consecutive lots or receive only a small number of the production lots, interpretation of trend may require addition information (e.g., yearly product report).
  4. In the case of imported vaccines, any available lot release certificate issued by the responsible NRA/NCL from the producing country can be used.
  5. A need for independent testing should be carefully considered in the establishment of the lot release procedures.

Regulatory Compliance: NMRA Lot Release Program

- **Key elements**
  - All vaccines must to go through the Lot Release Program prior to marketing
  - RSS activities include:
    - Capacity building and product quality assurance program and post-market activities
    - Improving co-ordination & collaborate between stakeholders

Regulatory compliance: Risk-based Lot Release Program

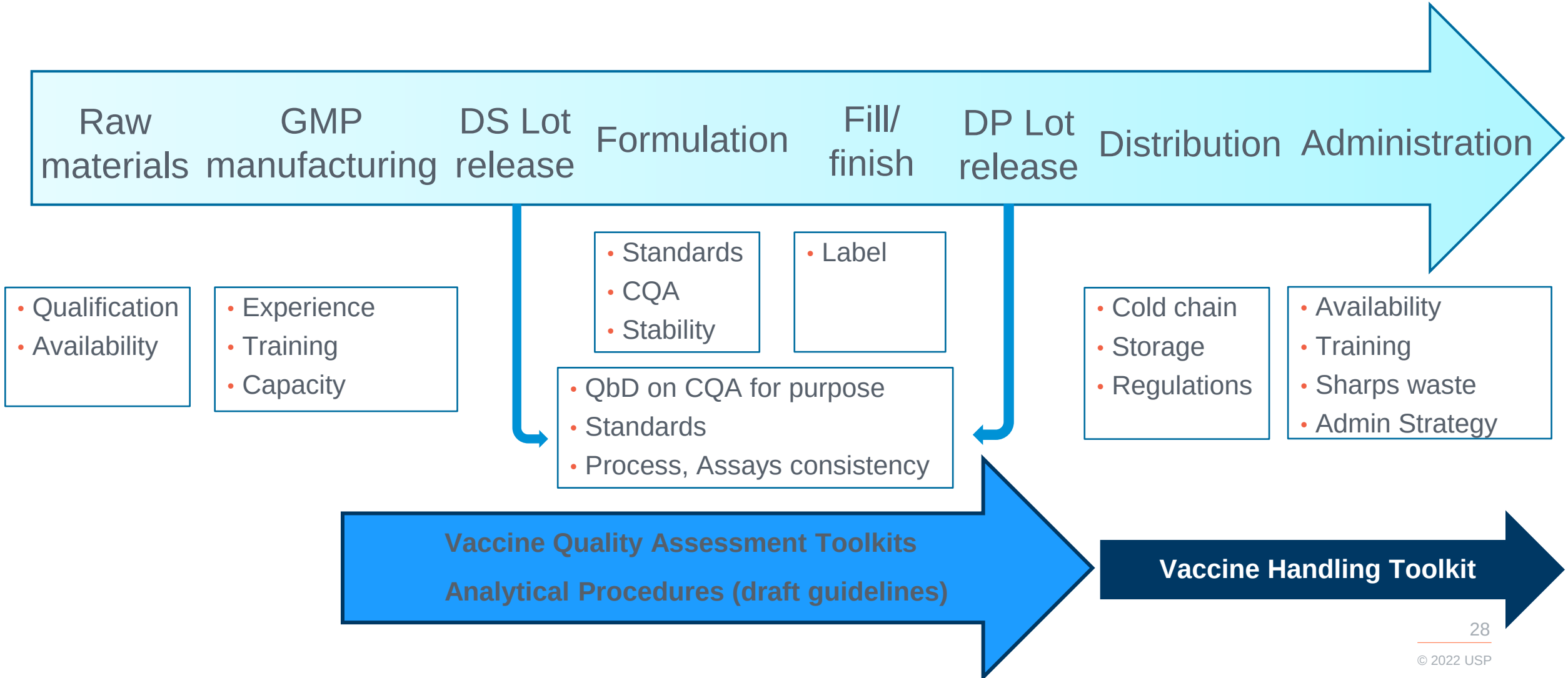
- **Risk-based lot release can be classified into four groups:**
  - Group 1A/1B - Pre-market only: clinical lots, consistency lots
  - Group 2 - Lab testing and protocol review
  - Group 3 - Protocol review
  - Group 4 - Periodic testing

Vaccines Technologies: Access, Manufacturing Challenges, and New Perspectives

Fouad Atouf, Ph.D.
Vice President, Global Biologics

Supporting Vaccine Quality

Potential risks to vaccine manufacturing and distribution



Vaccine quality assessment toolkits
Lessons from our work on Covid-19 vaccines

WHO advises that vaccines procured from assured sources are not tested again by receiving countries as they have been tested and released already by national regulatory authorities.

Guidance on developing a national deployment and vaccination plan for COVID-19 vaccines. WHO 1 June, 21

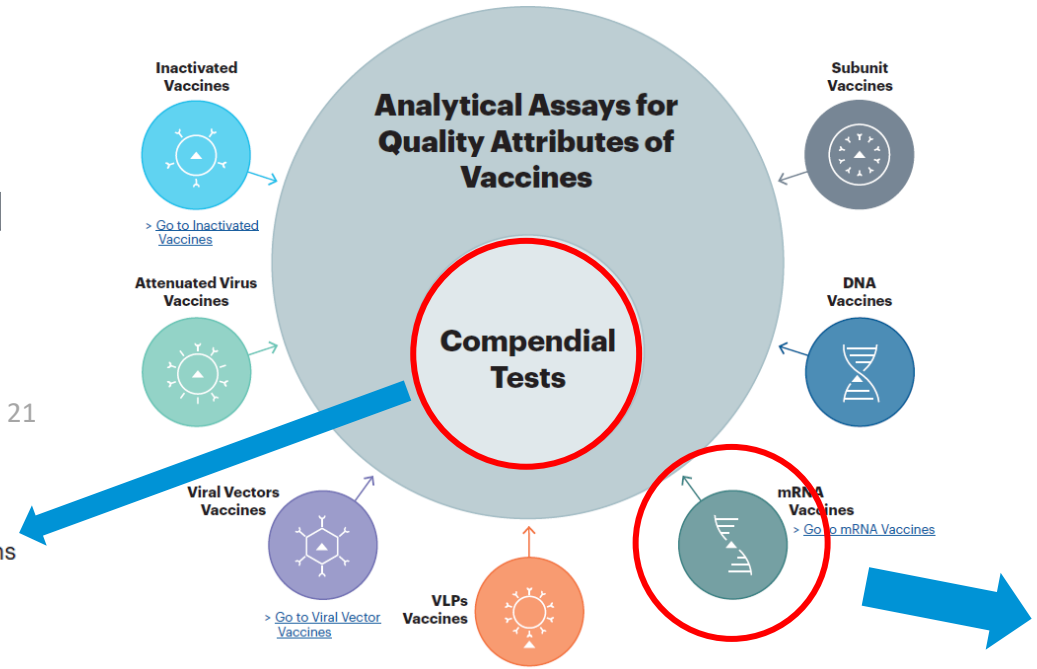
https://www.who.int/publications/i/item/WHO-2019-nCoV-Vaccine_deployment-2020.1

Compendial Tests
that may be applicable to most Vaccine Platforms

Attribute	USP chapters
Appearance	<1>, <790>
pH	<791>
Osmolality and Osmolarity	<785>
Container Closure Integrity	<1207>
Container Content for Injections *(includes extractable volume)*	<697>
Sterility	<71>
Bacterial Endotoxins	<85>

Platforms being used to develop vaccines against COVID-19

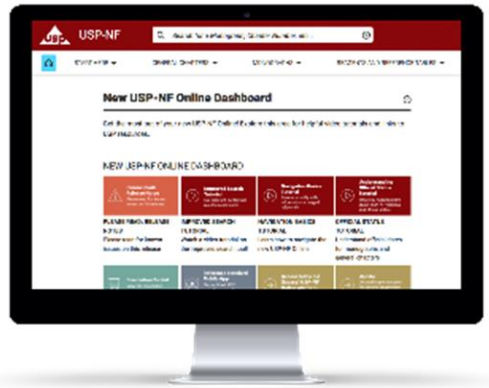
Toolkits for additional platforms will be added as these vaccines are authorized for COVID-19



https://www.usp.org/covid-19/quality-attributes-toolkits

USP documentary standards provide information regarding the tests that may be used to release vaccines. Can be helpful for interpreting data in lot release certificates.

USP-NF



Toolkit for Assessing Quality Attributes: mRNA Vaccines

Category	Attribute	Possible Methods[2]	Resource
Identity[1]	Sequence Confirmation	Sequencing	<1125>, <1126>
		RT-qPCR	<1126>, <1127>
Purity	RNA Integrity	CGE	<1053>
		Agarose Gel Electrophoresis for nucleic acids	<1126>
	Product-related impurities	IP-RP-HPLC	<621>
Potency[3]	Antigen expression	Western blot	<1104>
		Flow cytometry	<1027>
		Other cell-based assays	<1032>, <1033>, <1034>
Concentration	RNA Content	RT-qPCR	<1127>
		Fluorescence spectroscopy	<853>
		UV Absorbance	<857>
		Anion exchange chromatography	<1065>
Particle Size	Nanoparticles	Light Scattering	<1430.2>, <1430.3>, <1430.5>, <1430.6>

Building on USP biologics portfolio, and expanding the work on vaccines

Conventional Vaccine Platforms

- Reference standards and materials to measure quality of:
  - Adjuvants, carrier proteins, splitting agents,
- Documentary standards
  - New general chapters to support analytical methods e.g., molecular sizing for polysaccharide and glycoconjugate vaccines

mRNA Vaccines

- Collaborations on methods and materials
  - Raw Materials
  - mRNA Quality Attributes
  - Impurities

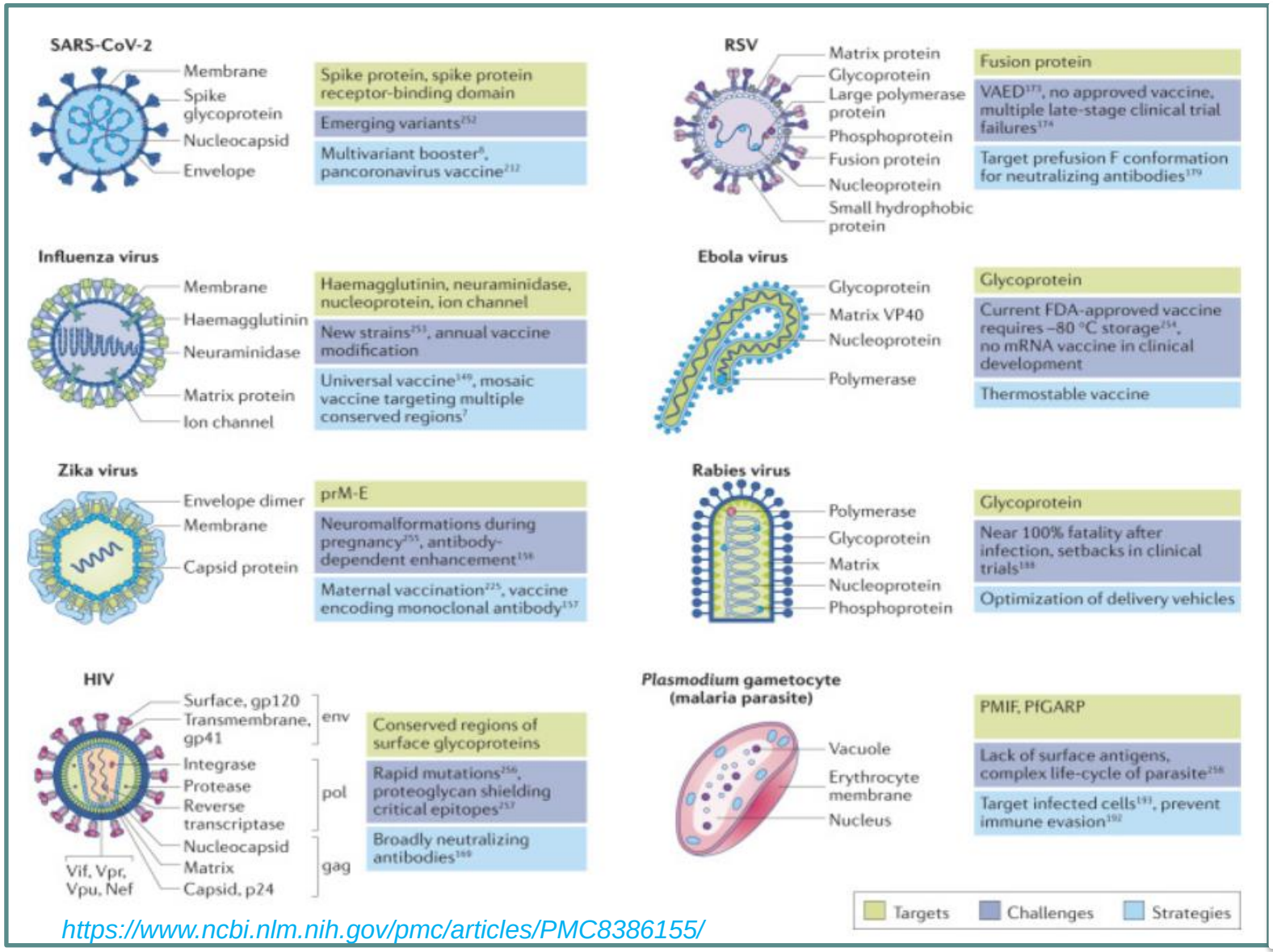
Viral Vectored Vaccines

- Initiating work with manufacturer on methods and materials
- Materials to demonstrate identity, purity, quantity

Ultimately working towards providing validated methods and associated reference materials to support vaccine quality

Available Online at: www.usp.org/mrna-quality and www.usp.org/viral-vectors

mRNA Vaccines – Beyond SARS-CoV-2



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8386155/

- mRNA therapies can protect against a wide variety of infectious pathogens and cancer using disease-specific targeting strategies
- mRNA requires safe, effective and stable delivery systems to protect the nucleic acid from degradation and allow cellular uptake and mRNA release
- Lipid nanoparticles (LNPs) have emerged as an effective vehicle to deliver COVID-19 vaccines and a variety of other therapeutics
- Aside from LNP, buffers, antioxidants, non-reducing free radical scavengers– all can be used to improve stability of the mRNA therapeutics

Our work on vaccines is integrated in the overall biologics strategy

Proteins / mAbs

- Measurement of critical quality attributes
- Best practices and analytical chapters

Cell and Gene Therapy (CGT)

- Viral vectors e.g., AAV, Lentivirus
- Nucleic acid testing
- Flow Cytometry
- Raw materials

Oligonucleotides

- Analytical methods
- Building blocks, raw materials

Vaccines

- Quality of vaccines components
- Impurities
- Tests to help with new modalities and platforms

Impurities

- Trace Metals
- Host cell proteins
- Residual DNA

Biomarkers

- Focus on established biomarkers, e.g., Type I diabetes, Kidney safety markers
- Biomarkers standards for early drug development

Genomics

- Data analysis
- Reagent and assays
- Precision Medicine decisions

Microbiology

- Rapid micro methods (RMM)
- Microbial testing and environmental monitoring

Support development, manufacturing, and global distribution of vaccines

Standards Initiatives

- Standards, publications, Product class approach – address quality attributes for classes of vaccines: subunit protein, DNA**, mRNA, and viral vector-based vaccines**
- Quality of vaccines components – raw materials, carrier proteins and adjuvants

Capability Building Initiatives

- Education and training to support development and manufacturing
- Collaborate with government agencies to ensure supply of high-quality vaccines
- Facilitate adoption of new technologies

Advocacy Initiatives

- Building and maintaining public trust in vaccines
- Adhering to scientifically based public health policies for equitable distribution of vaccines
- Improving the resilience of the supply chain, including for vaccines

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Empowering a healthy tomorrow