

CEPI



# CMC Comparability Workshop

September 28, 2020

# Agenda

6:00 Brief overview of structure, interactions and goals of COVAX facility/SWAT (manufacturing)/RAG-regulators (15 mins)

- Members of SWAT Core Team

6:15 Rationale for Request Regarding Comparability: Complexity, Concerns, Urgency (30 mins)

- Comparability Authorship Team led by Cristiana Campa (GSK)

6:45 Potential Approaches and Agreement Requested (45 mins)

- Comparability Authorship Team led by Cristiana Campa (GSK)
- C. Campa to lead discussion seeking input from workshop participants

7:25 Meeting wrap-up/notification of next workshops

# Our goals

To support the largest actively managed portfolio of vaccine candidates globally

To deliver 2 billion doses by end of 2021

To offer a compelling return on investment by delivering COVID-19 vaccines as quickly as possible

To guarantee fair and equitable access to COVID-19 vaccines for all participants

To end the acute phase of the pandemic by the end of 2021



# The COVAX Facility serves all participants

The COVAX AMC is an instrument for ODA-eligible countries

For all participants

The COVAX Facility

The AMC 92  
*ODA supported*

For ODA-eligible participants

**Higher Income Economies: 67**

Commitment Agreements (38) + team  
Europe (29), over 1 B people

**LIC/LMIC: 92 AMC-eligible economies<sup>1</sup>, 3.8+ B people**

**R&D: 9 CEPI-supported candidates, 9 BMGF-  
supported candidates under evaluation, and  
procurement conversations ongoing with additional  
producers**

**Manufacturers: 13 vaccine manufacturers across  
Asia, Europe and S. America <sup>2</sup>**

## Countries, R&D and manufacturers

# Comparability Challenges

# Manufacturing Changes Happen...

- Manufacturers of biotechnological/biological products frequently make **changes to manufacturing processes of products both during development and after approval.**
- When changes are made to the manufacturing process, the manufacturer generally evaluates the relevant quality attributes of the product to demonstrate that modifications did not occur that would adversely impact the safety and efficacy of the drug product.

# Comparability

- Comparability “ ... does not necessarily mean that the quality attributes of the pre-change and post-change products are identical, but that they are highly similar and that the existing knowledge is sufficiently predictive to ensure that **any differences in quality attributes have no adverse impact upon safety or efficacy of the drug product.**” [ICH Q5E]
- Generally, quality data on the pre- and post-change product are generated, and a comparison is performed that **integrates and evaluates all data collected**, e.g., routine batch analyses, in-process control, process validation/evaluation data, characterization and stability, if appropriate.
- The comparison of the results to the predefined criteria should allow an objective assessment of whether the pre- and post-change product are comparable.



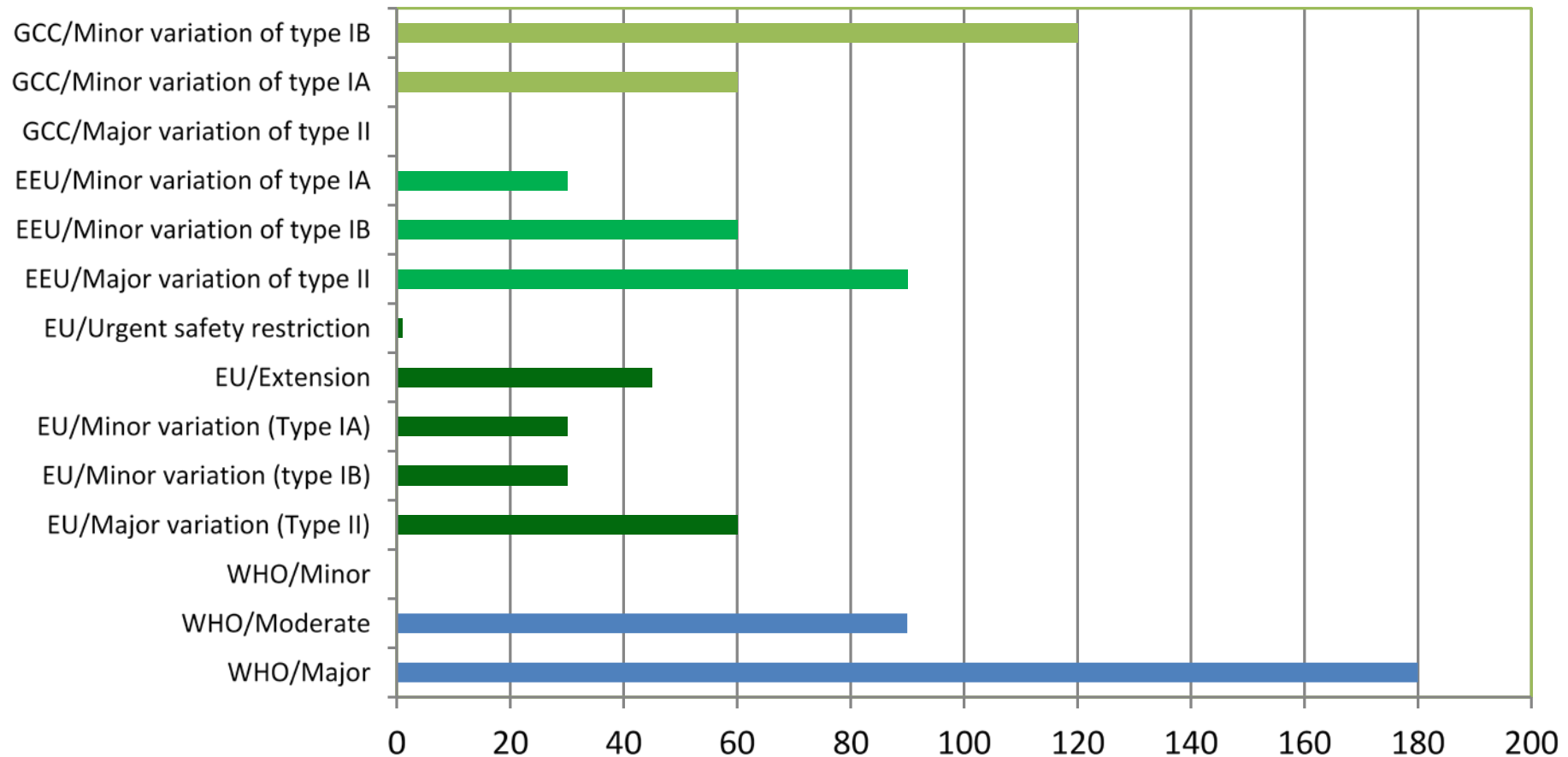
# Vaccine Complexity

- Manufacturing processes for COVID-19 vaccines are moving swiftly
  - Execution of process development with considerably reduced timelines
  - Evolving knowledge on product, analytics and process
  - Potential deferral of activities (e.g., optimization/ validation) until after launch to minimize timeline
- To make billions of doses, post-launch supply will likely require:
  - Use of multiple manufacturing sites
  - Need for many post-approval changes
- For manufacturing changes:
  - Need to show post-change product is comparable to the pre-change product
  - Ensure that the pre- and post-change products perform equivalently

# Concerns with Comparability

- Risk, and regulatory acceptability, depend on:
  - complexity and understanding of product and process
  - prior knowledge of platform, process and product
- But number of batches used in the clinic at accelerated pace results in limited historical data set to establish statistically based acceptance criteria
- Building strong, quality risk-based comparability strategies is key to support fast access to vaccines and sustainable lifecycle management
- To complicate matters further, current approaches to comparability and burdens of proofs for comparability vary greatly from country to country, as do approval timings → potential delay of access to vaccines

# Days for approval of PACs recommended by regulatory guidance from regional or international agencies



PAC: Post-approval Changes, GCC: Gulf Cooperation Council, Eurasian Economic Union, EU: European Union, WHO: World Health Organization

# Comparative analysis of the classification of selected examples of changes as per regional specific guidelines

Changes	Classification			
	WHO	EU	EEU	GCC
Change in the manufacturing process of the finished product (excluding scale up)	Moderate	Major (Type II)	Major (type II)	Major (type II)
Generation of a new Master Cell Bank (MCB) from same /different expression construct	Moderate	Major (Type II)	Extension to Market Authorization	Not covered in the PACs guideline
Change in the manufacturing process of diluent	Moderate / minor	Not covered in the PACs guideline	Minor (type IB)	Minor (type IB)
Qualification of a new reference standard	Moderate	Not covered in the PACs guideline	Not covered in the PACs guideline.	Not covered in the PACs guideline

# Urgency of Request

- Given the challenges associated with the COVID-19 emergency, comparability assessment may be on the critical path to ensure that COVID-19 vaccine is available to supply global patients
- Questions of comparability will need to be satisfied rapidly as Supply chains are expanded (scaled up and out)
- Cross-industry reflection and engagement of Regulatory Agencies is of outstanding importance, as it may provide a structured set of options to be rapidly assessed for the individual platforms/products
- To avoid delay or vaccine shortages, an agreed position on comparability for COVID-19 vaccines is required **by 4Q2020**, to maintain pace with the timelines needed to broaden availability of COVID-19 vaccines globally

# Potential Approaches to Demonstration of Comparability

- A risk-based analytical comparability assessment of manufacturing changes, to evaluate a subset of Critical Quality Attributes that are impacted by the proposed changes
- The use of release, forced degradation and/or characterization data to demonstrate comparability
- Key attributes linked to the pivotal study in which clinical efficacy has been demonstrated could be used to compare lots
- Where prior knowledge is limited and/ or in the absence of statistically based acceptance criteria, a “clinical development” type approach to comparability may be appropriate, aimed at demonstrating the preservation of quality attributes without the requirement of process consistency (in line with ICH Q5E)
- Global use of general/broader Post-approval Change Management Protocols (PACMPs) for routine changes

# Agreement Requested

- Risk-based analytical comparability assessments of the subset of CQAs that are impacted by the proposed changes
- Use of release, forced degradation and/or characterization data to demonstrate comparability
- Use of post-change lots to be compared to lots used in pivotal clinical studies
- In cases where prior knowledge is limited, and when there is no statistical basis for acceptance criteria due to limited number of lots, use of approaches to comparability focused on product quality expectations
- Early feedback from regulatory authorities for comparability approaches in advance of obtaining efficacy data from Phase 3 to help confirm requirements and ensure alignment on product specific approaches.
- Global Use of general/ broader PACMP for routine changes/ introduction of multiple manufacturing processes
- A harmonized single approach to comparability amongst nations

# Wrap-up and Upcoming Workshops

## **Thursday October 8<sup>th</sup>** – RAG Feedback Workshop

- *7-9AM PST, 10AM–12PM EST, 16-18PM CEST*
- Topics with RAG Feedback: Process validation, Expiry, Labeling, Post approval changes, National lab testing

## **Monday October 26<sup>th</sup> (to be confirmed)**- Accelerated Vaccine Development & EUL Best Practices Workshop

- *6-8AM PST, 9-11AM EST, 15-17CEST*
- Topics: Lessons learned preparing vaccine in response to epidemics (nOPV2, Ebola, H1N1), Guidance on WHO's EUL Process