Mitigating impact of SARS-CoV-2 pandemic on available supply for commercialization and programmatic doses required of non-COVID-19 vaccines

Methodology

Introduction

In the context of the COVID-19 pandemic and the unprecedented efforts to develop, manufacture, and deliver large quantities of COVID-19 vaccines, the global programmatic doses requirement (PDR) for non-COVID-19 vaccines has been impacted. In parallel risks have emerged for the global supply for these vaccines.

In 2021, the World Health Organization (WHO), as part of the Market Information for Access (MI4A) project, has sought to assess the potential risks and impacts of the SARS-CoV-2 pandemic and COVID-19 vaccine manufacturing and implementation on PDR and vaccine production.

The analysis was conducted leveraging information collected consultations with WHO Regional and Country Offices, partners1- several experts and vaccine manufacturers as well as the convening of separate workshops to explore the potential impact and risks and discuss mitigating actions. The public summary of the analysis will be published by end of year on the MI4A website.

Analysis on the impact of the COVID-19 on demand

The analysis on the impact of the COVID-19 pandemic and introduction of COVID-19 vaccines on demand was conducted based on the following:

1. Bilateral consultations with key experts at global and regional levels

A set of exploratory consultations was conducted to 1) understand how potential factors related to COVID-19 pandemic can impact vaccine demand (estimated doses) of immunization programmes; and 2) Understand the impact on global mid/long-term demand (forecasting purposes, considering a 10-year horizon). The scope of the consultations focused on all major vaccines in the routine programme: BCG, D&T, MCV, HPV, Pneumococcal, Rotavirus and Polio vaccines (IPV and OPV). Individuals consulted are included as part of Annex 1.

2. Online survey of WHO and UNICEF regional and country offices representatives

An online survey was developed and sent to WHO and UNICEF regional offices to be shared to relevant staff at the regional level and in countries to obtain feedback on the factors identified through the consultations. Responses were received mainly from 5 out of 6 WHO regions. (Survey questions are included in Annex 2)

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1 Partners included in consultations included: independent vaccine manufacturing experts, WHO, UNICEF, CEPI, Gavi, BMGF, Wellcome Trust, CHAI as well as industry associations
3. **Vaccine specific workshops**

WHO organized vaccine specific workshops on BCG, D&T, MCV, HPV, Pneumococcal, Rotavirus and Polio vaccines (IPV and OPV). The meetings brought together WHO Regional colleagues and key partners (UNICEF, Gavi, BMGF) to determine the directional impact of the pandemic on vaccine dose requirements for the mid-to-long-term and related risks and possible mitigation measures.

**Analysis on the impact of the COVID-19 on supply**

The analysis on the impact of the COVID-19 pandemic and production of COVID-19 production on vaccine supply for other antigens was conducted based on the following:

1. **Industry Data Collection**

Vaccine Manufacturers were consulted through an online survey in January 2021. The objective of the survey was to estimate possible factors that could impact the production of non-COVID-19 vaccines because of the pandemic (survey questions are available as Annex 5).

2. **MI4A manufacturer survey**

Additional questions specific to this analysis were added to the yearly MI4A data collection form that is sent to manufacturers in Q2. Through this annual data collection effort, WHO collected information from 44% of vaccine manufacturers that represent over 90% of the global vaccine market (excluding COVID-19). WHO is therefore able to leverage data shared by manufacturers to produce estimates that are considered accurate.

3. **Expert Guidance**

Three multilateral workshops were convened by WHO in Q2 2021. The first two workshops focused on mapping the risks and impact of the pandemic on the manufacturing processes and related availability of non-COVID-19 vaccines. A third workshop was organized to review the identified risks and get expert feedback on potential measures to mitigate risks on production and availability of non-COVID-19 vaccines and avoid potential disruption to routine immunization programs. The feedback received was leveraged to build this analysis.

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1 Expert participants invited to participate to the workshops were asked to declare their interests and in accordance with WHO policy were approved to participate in these workshops.
ANNEXES

Demand Analysis

- Annex 1. List of individuals consulted
- Annex 2. WHO and UNICEF Regional and Country Offices online survey

Supply analysis:

- Annex 3. Workshop participants
- Annex 4. Workshop agendas
- Annex 5. Industry Data Collection survey and questions
- Annex 6. List of participating manufacturers

ANNEX 1. List of individuals consulted on demand

<table>
<thead>
<tr>
<th>First Name</th>
<th>Last Name</th>
<th>Organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Don Ananda</td>
<td>Chandralal Amarasinghe</td>
<td>WHO WPRO</td>
</tr>
<tr>
<td>Nuria</td>
<td>Amich</td>
<td>UNICEF</td>
</tr>
<tr>
<td>Karine</td>
<td>Amma El Kerdi</td>
<td>Gavi</td>
</tr>
<tr>
<td>Phionah</td>
<td>Atuhebwe</td>
<td>WHO AFRO</td>
</tr>
<tr>
<td>Ed</td>
<td>Baker</td>
<td>Gavi</td>
</tr>
<tr>
<td>Oleg</td>
<td>Benes</td>
<td>WHO EURO</td>
</tr>
<tr>
<td>Robin</td>
<td>Biellik</td>
<td>Independent</td>
</tr>
<tr>
<td>Paul</td>
<td>Bloem</td>
<td>WHO</td>
</tr>
<tr>
<td>Siobhan</td>
<td>Botswright</td>
<td>WHO AMRO</td>
</tr>
<tr>
<td>Maricel</td>
<td>Castro</td>
<td>WHO HQ</td>
</tr>
<tr>
<td>Thomas</td>
<td>Cherian</td>
<td>MMGH</td>
</tr>
<tr>
<td>Hans</td>
<td>Christiansen</td>
<td>UNICEF</td>
</tr>
<tr>
<td>Simon</td>
<td>Courbon</td>
<td>UNICEF</td>
</tr>
<tr>
<td>Natasha</td>
<td>Crowcroft</td>
<td>WHO</td>
</tr>
<tr>
<td>Niklas</td>
<td>Danielsson</td>
<td>UNICEF</td>
</tr>
<tr>
<td>Carolina</td>
<td>Danovaro</td>
<td>WHO HQ</td>
</tr>
<tr>
<td>Shalini</td>
<td>Desai</td>
<td>WHO</td>
</tr>
<tr>
<td>Tondo Opute</td>
<td>Emmanuel Njambe</td>
<td>SEARO</td>
</tr>
<tr>
<td>Kamal</td>
<td>Fahmy</td>
<td>WHO RO</td>
</tr>
<tr>
<td>John</td>
<td>Fitzsimmons</td>
<td>WHO AMRO</td>
</tr>
<tr>
<td>Abraham</td>
<td>Kofi Ntow</td>
<td>UNICEF</td>
</tr>
<tr>
<td>Solo</td>
<td>Kone</td>
<td>WHO HQ</td>
</tr>
<tr>
<td>Scott</td>
<td>LaMontagne</td>
<td>PATH</td>
</tr>
<tr>
<td>Samya</td>
<td>Mandal</td>
<td>Gavi</td>
</tr>
</tbody>
</table>
ANNEX 2. WHO and UNICEF Regional and Country Offices online survey

Please indicate if you work for WHO or UNICEF

Please indicate your country of employment.

Region Based on your opinion, for the following five factors, please select their likelihood of occurrence over the next 12-18 months.

- Disruptions in the provision of routine immunization services
- Disruption in provision of vaccination campaigns
- Changes in health seeking behaviors (e.g., reduced access due to shutdowns, scared to go out due to contracting SARS-CoV-2)
- Disruption of immunization staff and workforce (e.g., reduction in staff or reallocation of staff to respond to SARS-CoV-2)
- Changes to the supply and cold chain (e.g., transportation issues, increased open or closed wastage, decreased cold chain space)
- Decreased financial support for immunization programmes

Based on your opinion, for the following five factors, please select their anticipated magnitude of impact on vaccine demand (in doses), considering the next 12-18 months:

- Disruptions in the provision of routine immunization services
- Disruption in provision of vaccination campaigns
- Changes in health seeking behaviors (e.g., reduced access due to shutdowns, scared to go out due to contracting SARS-CoV-2)
- Disruption of immunization staff and workforce (e.g., reduction in staff or reallocation of staff to respond to SARS-CoV-2)
- Changes to the supply and cold chain (e.g., transportation issues, increased open or closed wastage, decreased cold chain space)
- Decreased financial support for immunization programme

Please add any other factors that you believe could impact vaccine use (in doses) over the next 12-18 months.
Please select all of the vaccines that you would like to answer questions about. Note that the remainder of this survey is designed to only show specific questions related to the vaccines that you select in this question.

For the following vaccines, please indicate which of the identified factors that you anticipate:

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG</td>
<td>• Disruptions in the provision of routine immunization services</td>
</tr>
<tr>
<td>DTP</td>
<td>• Disruption in provision of vaccination campaigns</td>
</tr>
<tr>
<td>Pneumococcal Vaccines</td>
<td>• Changes in health seeking behaviors (e.g., reduced access due to shutdowns, scared to go out due to contracting SARS-CoV-2)</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>• Disruption of immunization staff and workforce (e.g., reduction in staff or reallocation of staff to respond to SARS-CoV-2)</td>
</tr>
<tr>
<td>Measles Containing Vaccines (MCV)</td>
<td>• Changes to the supply and cold chain (e.g., transportation issues, increased open or closed wastage, decreased cold chain space)</td>
</tr>
<tr>
<td>HPV</td>
<td>• Decreased financial support for immunization programme</td>
</tr>
<tr>
<td>OPV</td>
<td></td>
</tr>
<tr>
<td>IPV</td>
<td></td>
</tr>
</tbody>
</table>

For the vaccines listed (BCG, DTP, Pneumococcal Vaccines, Rotavirus, MCV), HPV, OPV, IPV) do you anticipate that supplemental immunization activities, requiring a significant amount of vaccine doses, will be needed over the next 12-18 months to catch-up children missed by routine immunization due to the pandemic?

For the vaccines listed and in your opinion, please indicate how planned routine introduction will be impacted over the next 12-18 months:

- DTP boosters
- Rotavirus
- Pneumococcal
- MCV (2nd dose)
- HPV

For the vaccines listed below and in your opinion, please indicate how planned supplementary immunization activities will be impacted over the next 12-18 months:

- MCV
- Polio

Based on your opinion, what will be the impact of SARS-CoV-2 pandemic on future coverage levels compared to pre-pandemic coverage levels over the next 12-18 months?

- BCG coverage levels
- DTP1 coverage levels
- DTP3 coverage levels
- D&T booster coverage levels
- PCV3 coverage levels
- Rota last dose coverage levels
- MCV1 coverage levels
- MCV2 MSIA coverage levels
• HPV coverage levels
• Polio3 coverage levels
• IPV coverage levels

Based on your opinion, please indicate how future wastage rates compared to pre-pandemic wastage levels may be impacted over the next 12-18 months.

• Changes in closed vial wastage due to expiration issues
• Changes in open vial wastage for BCG 20-dose vials due to less individuals immunized during sessions
• Changes in open vial wastage for BCG 10-dose vials due to less individuals immunized during sessions
• Changes in open vial wastage for MCV 10-dose vials (during routine immunization) due to less individuals immunized during sessions

ANNEX 3. Workshop Participants

The following stakeholders attended one or more workshops. Manufacturers attended only the first workshop.

World Health Organization (WHO)
• Tania Cernuschi, Team Lead Global Access, Immunization, Vaccines, and Biologicals (IVB)
• Johanna Fihman, Technical Officer Global Access, IVB
• Martin Friede, Unit Head, Vaccine Product & Delivery Research, IVB
• Joachim Hombach, Senior Health Adviser, Team Lead Policy, IVB
• Ann Lindstrand, Coordinator Expanded Programme for Immunization, IVB
• Kate O’Brien, Director, IVB
• Carmen Rodriguez, Group Lead, Vaccines Assessment, Prequalification, IVB

Vaccine manufacturers (March 5th workshop only)
• BioFarma and Serum Institute of India, representing the Developing Country Vaccine Manufacturers Network
• Merck and Sanofi Pasteur, representing the International Federation of Pharmaceutical Manufacturers and Associations

Independent experts
• Raafat Fahim, President and CEO, REF Consulting
• Shanelle Hall, Founder Member, The Yellow House
• Kristopher Howard, Consultant, NRL Solutions
• Craig Laferrière, Head Vaccine Development, Novateur Ventures Inc.
• Vittoria Pellegrini, Consultant
• George Robertson, Chief Scientific Officer, Cambra Consulting Inc.
• Jim Robinson, Principal, James Robinson Biologics Consulting
• Rahul Singhvi, Co-founder and CEO, National Resilience Inc.
• Gerd Zettlmeissl, Consultant, Former CEO Valneva SE (formerly Intercell AG) Vienna, Austria

Observers from partner organizations
• Pan-American Health Organization Revolving Fund (PAHO RF): Siobahn Botwright, John Fitzsimmons and Murat Ozturk
- Coalition for Epidemic Preparedness Innovations: Matthew Downham, and Nicole Laurie
- Bill & Melinda Gates Foundation: Peter Dull, Helen Matzger, and David Robinson
- Clinton Health Access Initiative: Wrick Ghosh and Frauke Uekermann
- Gavi, the Vaccine Alliance: Dominic Hein
- Wellcome Trust: Freya Hopper
- UNICEF: Hanne Bak Pederson, Andrew Jones, and Yalda Momeni

Meeting facilitated by MM Global Health Consulting (MMGH, Stefano Malvolti, Melissa Ko, Adam Soble) with support from Fondazione Sclavo (Gianluca Breghi)

**ANNEX 4. Workshop Agendas**

<table>
<thead>
<tr>
<th>Workshop #1 – March 5th, 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>15:00 – 15:15</td>
</tr>
<tr>
<td>15:15 – 15:30</td>
</tr>
<tr>
<td>15:30 – 15:50</td>
</tr>
</tbody>
</table>
| 15:50 – 16:30 | 4. Validation of the mapping of vaccine manufacturing activities impacted by SARS-CoV-2 pandemic and COVID-19 vaccine development and production  
*Goal: Identify the impacted vaccine manufacturing activities* | Manufacturers / Experts |
| | Facilitation: MMGH | |
| 16:30 – 17:00 | 5. Discuss and identify associated risks and implications of impacted vaccine manufacturing activities  
*Goal: Detail the potential risks of different impacted vaccine manufacturing activities* | Manufacturers / Experts |
| | Facilitation: MMGH | |
| 17:00 – 17:05 | Coffee break | |
| 17:05 – 18:00 | 6. Brainstorm possible risk mitigation measures for impacted vaccine manufacturing activities  
*Goal: Agree on possible mitigation measures* | MMGH / All |
| | Meeting closure | |
### Workshop #2 – March 10th, 2021

<table>
<thead>
<tr>
<th>Time</th>
<th>Agenda</th>
<th>Facilitator</th>
</tr>
</thead>
<tbody>
<tr>
<td>15:00 - 15:10</td>
<td>1. Objectives of the meeting &amp; introduction of participants</td>
<td>WHO</td>
</tr>
</tbody>
</table>
| 15:10 – 15:30 | 2. Review of outputs from Meeting #1  
   *Goal: Refresh participants on key discussions and outputs from Meeting #1* | MMGH        |
| 15:30 – 15:50 | 3. Manufacturer updates from                                           | Workshop participants |
| 15:50 – 16:10 | 4. Refine mapping of vaccine manufacturing activities impacted by SARS-CoV-2 pandemic and COVID-19 vaccine development and production  
   *Goal: Refine Meeting #1 outputs* | Experts Facilitation: MMGH |
| 16:10 – 18:00 | 5. Identify vaccines most likely impacted and estimate high-level impact to the supply and availability of each vaccine (with focus on BCG, D&T containing, Pneumococcal, Measles-containing, HPV) and discuss specific risks and mitigations  
   *Goal: Agree on vaccines most likely impacted and estimate the scale of the impact for each vaccine* | Experts Facilitation: MMGH |

### Workshop #3 – May 26th, 2021

<table>
<thead>
<tr>
<th>Time</th>
<th>Agenda</th>
<th>Facilitator</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:30 – 14:45</td>
<td>1. Objectives of the meeting &amp; introduction of participants</td>
<td>WHO</td>
</tr>
<tr>
<td>14:45 – 15:00</td>
<td>2. Update on ongoing manufacturing capacity initiative and potential impacts on non-COVID-19 vaccines and implications for supply availability</td>
<td>CEPI/WHO on behalf of COVAX Joint Manufacturing Taskforce</td>
</tr>
<tr>
<td>15:00 – 16:30 (including 10 min break)</td>
<td>3. Review of market overviews and estimated supply impact for BCG, D&amp;T containing, Pneumococcal, Measles-containing, HPV, Rotavirus and Polio vaccines</td>
<td>WHO MMGH</td>
</tr>
</tbody>
</table>
4. Identify mitigation measures for vaccines most impacted/likely to be impacted

ANNEX 5 – Industry Data Collection

Table 1. Data collected in initial outreach

1. Do you expect impact from the SARS-CoV-2 vaccine and COVID-19 development efforts on your available supply for commercialisation for commercialised products and products about to be registered for 2021, 2022 and 2023? Which products and what order of magnitude?

2. What are the main constraints affecting the input to your production processes (e.g. access to ingredients, single use components, containers etc. or issues with workforce availability)?

3. What are the main constraints linked to your manufacturing processes (e.g. repurposing of bulk production equipment/workforce/CMOs/fill & finish lines/quality labs for COVID-19 vaccine production)?

4. What are the main constraints in the release and distribution of the vaccines produced (e.g. disruptions in transportation/lot releases; constraints in warehousing and freight forwarding)?

Table 2. Data collected in manufacturer survey

<table>
<thead>
<tr>
<th>PRODUCT INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Product Name(s): Provide the brand name of the product, its clinical trial identifier, or its generic name - if multiple names exist, please indicate all the names</td>
</tr>
<tr>
<td>2. Indication: Provide the diseases for which the vaccine is indicated, if possible, please list the age range(s)</td>
</tr>
<tr>
<td>3. Antigen: List all antigens contained in the vaccine</td>
</tr>
<tr>
<td>4. Presentation - container: List separately in one row all that are available e.g., Vial, PFS, Ampoule</td>
</tr>
<tr>
<td>5. Presentation - number of doses: List separately in one row all that are available e.g., 1-dose, 5-dose, 10-dose</td>
</tr>
</tbody>
</table>

MANUFACTURING PROCESS INFORMATION
**6. Other product(s) sharing manufacturing process/ingredients:** For each product, list any other products whose source of specific ingredients is common (e.g., DTP and Pentavalent) or that utilise part of the same manufacturing facility.

**7. Plant(s) location (City, Country):** Provide the city and country where the following production phase is performed for (a) drug substance, (b) drug product, (c) filling & finishing.

**PRODUCT STATUS INFORMATION**

**8. Releasing National Regulatory Authority (NRA):** Provide the national authority/ies in charge of releasing the product for export.

**9. Product Status:** (a) Indicate the product status -- (Marketed, Licensed, In development); (b) if in development, indicate the phase (pre-clinical, Phase I, Phase II, etc).

**10. Year of First Registration / Expected Year of Registration:** Indicate the year of first registration with a NRA or for products in development, indicate the expected year for registration.

**11. Year of WHO Prequalification (PQ) / Expected Year of WHO PQ:** Indicate the year when WHO PQ was awarded (NA if not PQed); for products in development, indicate the year when WHO PQ is expected (NA if there are no plan for PQ).

**12. Status change:** For each product, indicate any recent or expected status changes (e.g., move to a next development phase, product withdrawal, re-enter into the market) and the timing for the change.

**AVAILABLE DOSES FOR COMMERCIALIZATION DATA -- provide one number for the stated timeframe**

**13. Maximum doses available for commercialization:** The maximum annual number of doses that could be made available for sale during 2021-2026.

**14. Average doses available for commercialization:** The average annual number of doses expected to be available for sale of that specific product during 2021-2022.

**15. Minimum doses available for commercialization:** The minimum annual number of doses that could be made available for sale during 2021-2026.

**SARS-CoV-2 IMPACT**

**16. SARS-CoV-2 pandemic impact on average doses available for commercialization for existing operations:** Has the SARS-CoV-2 pandemic impacted the average annual number of doses expected to be available for sale of that specific product during 2021-2022 (Y/N).

**17. COVID-19 vaccine development impact on average doses available for commercialization:** Has COVID-19 vaccine development impacted the average annual number of doses expected to be available for sale of that specific product during 2021-2022 (Y/N).
18. Quantify in percentage how the average doses available for commercialization is impacted (e.g. -10%): By what percentage of annual number of doses expected to be available for sale of that specific product during 2021-2022

COMMENTS

19. Comments: any other relevant information can be included here

REGISTRATION AND COMMERCIALIZATION DATA (Please fill out this section in the 'Registration Status' tab. If it is easier, you may attach separately the information in another format)

- List of countries where the product is registered and sold directly by the company (R)
- List of countries where the product is registered and sold ONLY through a distributor (D)
- List of countries where the product registration is pending or planned (P)
- List of countries where product is registered and licensed to a third party (L)

COVID-19 VACCINE DEVELOPMENT

1. Are you developing and/or producing a COVID-19 vaccines (yes/no)? If yes, what is the product name?

2. If yes, what stage of development is the product in (e.g., pre-clinical, Phase 1, Phase 2, Phase 3, Licensed)?

COVID-19 VACCINE MANUFACTURING

3. Are you manufacturing COVID-19 vaccine(s) developed by another entity (yes/no)?

4. If yes, what is the COVID-19 vaccine product name and entity which originally developed the COVID-19 vaccine(s) that you are manufacturing?

5. What manufacturing activities are you performing for each of the COVID-19 vaccines being manufactured in your facilities (e.g., drug substance, drug product, fill/finish)?

6. Are you experiencing or expect to experience challenges in procurement of: (a) raw materials (b) components and consumables or (c) equipment for the production of COVID-19 vaccines or other antigens?
ANNEX 6. List of participating manufacturers

- AJ Biologics
- BB NCIPD Ltd.
- Beijing Minhai Biotec Group
- Bharat Biotech International Ltd.
- Biological E. Limited
- Biomanguinhos/Fiocruz
- CD BIO
- Daichi Sankyo
- Eubiologics
- Fundação Ataulpho de Paiva
- GSK
- HLL Biotech
- Incepta Vaccine Limited
- Indian Immunological Ltd.
- Innovax
- Institute of Vaccines and Medical Biologicals
- Japan BCG Laboratory
- Lanzhou Institute of Biological Products Co., Ltd
- MassBiologics
- Merck Sharp & Dohme Corp.
- Nignbo RongAn
- Panacea Biotec Limited
- Pfizer
- PT Bio Farma
- Queen Saovabha Memorial Institute (Thai Red Cross)
- Sanofi
- Serum Institute of India Ltd.
- Shanghai Zerun Biotech Co., Ltd.
- Shanghai Foxun
- Shantha
- Sinergium Biotech
- Sinovac Biotech Co. Ltd
- SK Biologics
- Takeda
- Tianjin CanSino Biotechnology Inc.
- The Biovac Institute
- Walvax Biotechnology Co., Ltd.
- Xiamen Innovax Biotech Co., Ltd.
- Zydus Cadila Group