COVAX Drug Product Workshop Part 2

Partner discussions on choice of vials and use of DP network

3 August 2020

Objectives for today

- The industry has an unprecedented challenge for emergency vaccine supply
- Global estimates for vaccine supplies exceed 4BN doses across multiple platforms by end 2021, and similar annual production thereafter
- At 4 BN doses per year:
  - 10.9M doses will be produced every day
  - 456,600 doses will be administered every hour
  - 7,610 doses filled and injected every minute
- This assumes 24 hours per day, 7 days per week and may need to be sustained for 2-3 years
- This is in addition to the 4-5BN doses of vaccine produced for routine use.

- Our goal is to maximize doses delivered in a compliant manner
- CEPI is prepared to support your important efforts with glass, stoppers, caps, and filling capacity if needed.

Agenda for today

- Introductions
- DP image choices
  - Interest in 10R or 20R vials secured by CEPI?
  - Interest in stoppers/caps?
  - Does CEPI need to investigate the vial adapter supply?
- DP Network Design
  - Interest in using this network?
  - Will we achieve critical volumes to support creation of the network?
- Discussion of next steps
- Conclusions

Attendees

- AAVCOVID/MEEI/Novartis
- AstraZeneca
- Bio Farma
- Biological E
- BMGF
- CEPI
- Clover
- CSL
- DCVMN
- FDA
- Gavi
- Icosavax
- IFPMA
- Merck
- MSF
- Novavax
- PATH
- PATH/ISMMS
- PATH/Mt. Sinai
- Serum
- UNICEF
- University of Queensland
- Vaccines Europe
- Walvax
- WHO
- Zhifei

DP Image Choices

10R vs 20R vials options and impact

Background

Earlier this year, we identified **>10BN doses of DS** capacity and **>4BN doses of capacity for glass vial filling** at 20-dose/vial

There appears to be **a severe, global limitation of tubing glass** – used for pharmaceutical vials

- We have reserved capacity at OMPI to support 100M 20R vials **or** 120M 10R vials (2020-2021). Mix of the two formats is possible but needs to be negotiated with the supplier
- We have been granted priority access to the capacity beyond 2021. Any vial size can be produced

We have agreed to develop smaller MDV images after peak demand for vaccine.

Not all partners will use CEPI's vial/DP network, **multiple MDV images may be deployed**, depending on which vaccines succeed (5-dose, 10-dose, 15 doses, 18 doses in a 10R vial).

Multi-dose vials (MDVs)

- Given current shortages in pharmaceutical glass, multi-dose vials (MDVs) will maximize the amount of vaccine available
- Long history of using MDVs in campaign settings

Multi-dose vials (MDVs)

- Initial response: **10, 15, 18, 20-dose tubing glass vials (to be determined)** for not preserved drug product; use within 6 hours of first dose
- After 12-18 months depending on demand shift to: **preserved multidose (5-10 dose/vials to be determined) for routine use/stockpile**
- Low-coring stopper design chosen
- Vial adapter option

Options to Consider for MDV

20R vial - filled to deliver 20 doses = 2.0 BN doses (before wastage)

10R vial – filled to deliver 10 doses = 1.2 BN doses (before wastage),

10R vial – filled to deliver 15 doses = 1.8 BN doses (before wastage)

10R vial – filled to deliver 18 doses = 2.16 BN doses (before wastage)

Options with more than 20 doses per vial not considered given higher wastage and possible coring (unless adaptor is used)

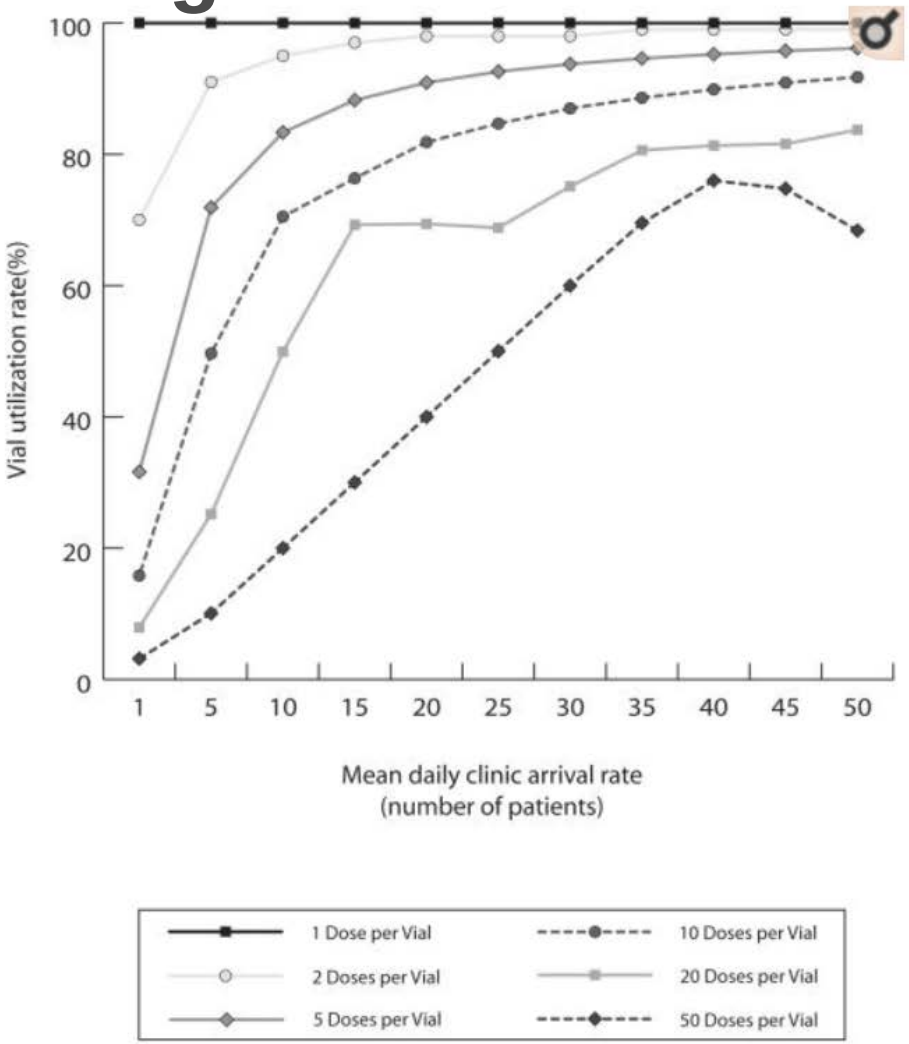
Options with less than 10 doses per vial not considered because of insufficient output

Capacity options* with current glass supply contract

Vial type	Vials available (million)	Doses/vial	Capacity (million doses)
10R	120	10	1200
10R	120	15	1800
10R	120	18	2160
20R	100	20	2000

* Available glass can support any one of these options or a proportional split of several options

Wastage



- The Figure shows how percentage of doses wasted (i.e., number of doses wasted/total number of doses) varies by the patient arrival rate.
- Each line represents a different vial presentation.
- As the patient arrival rate increases, the wastage rate for the multi-dose presentations decreases while the wastage rate for the single dose presentation remains constant

Single versus Multi-Dose Vaccine Vials: An Economic Computational Model

Bruce Y. Lee, MD, MBA,[1,2] Bryan A. Norman, PhD,[3] Tina-Marie Assi, MPH,[1,2] Sheng-I Chen,[3] Rachel R. Bailey, MPH,[1,2] Jayant Rajgopal, PhD,[3] Shawn T. Brown, PhD,[4] Ann E. Wiringa, MPH,[1,2] and Donald S. Burke, MD[2]

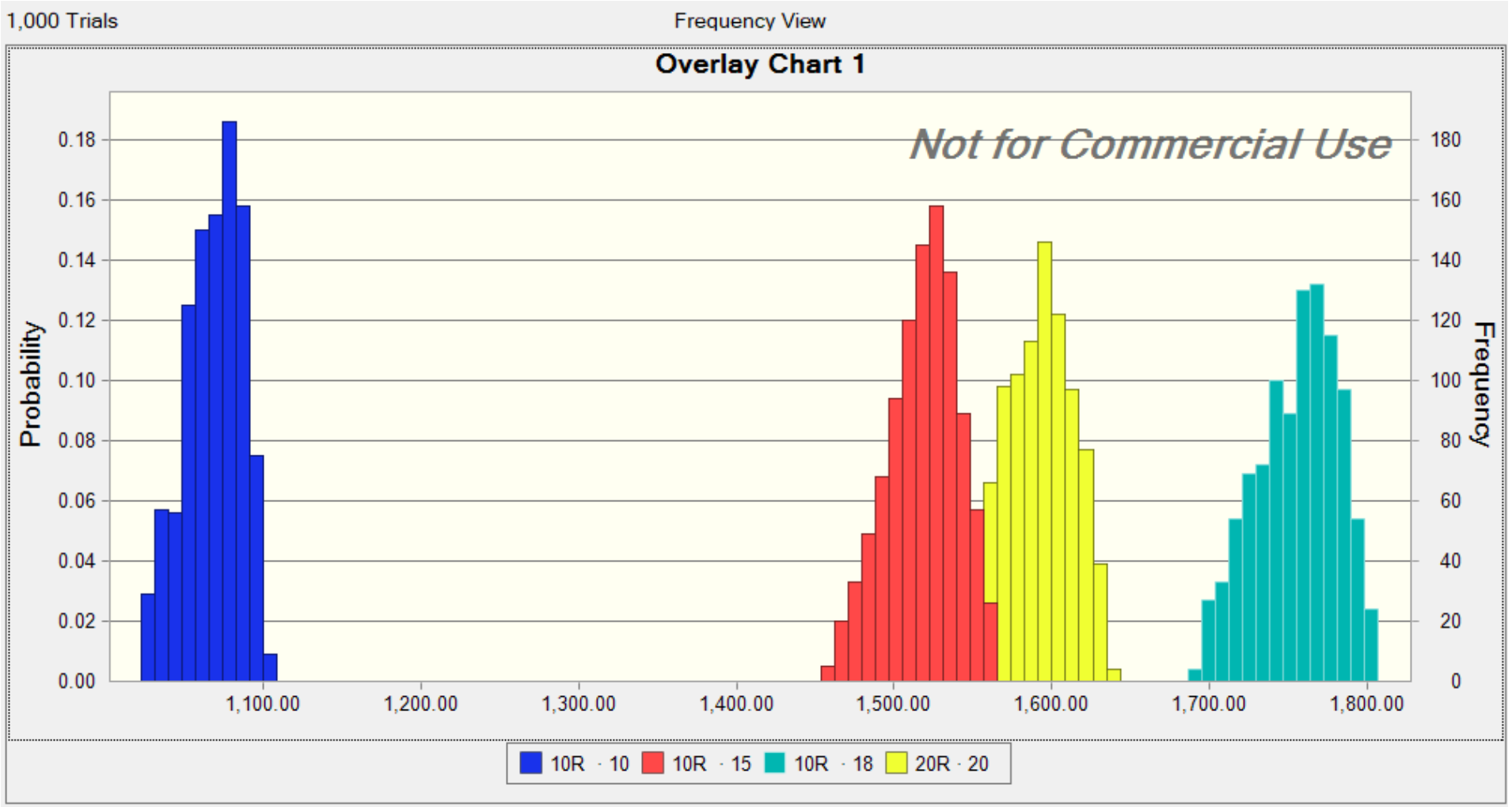
Vaccine. 2010 Jul 19; 28(32): 5292–5300.

Wastage adjusted doses

Vial type	Vials available (million)	Doses/vial	Capacity (million doses)	Waste (estimate 1)	Immunisations
10R	120	10	1200	0.10	1080
10R	120	15	1800	0.15	1530
10R	120	18	2160	0.18	1771
20R	100	20	2000	0.20	1600

Wastage increasing linearly between 10% and 20%

Monte Carlo simulation



Wastage variability: - 0.02 +0.04 point estimate value

Stoppers

- CEPI has completed an open tender for gamma irradiated ready-to-use rubber stoppers and aluminum caps

- Two low-coring stoppers are currently under evaluation:
  - Bromobutyl stopper (Aptar)
  - Chlorobutyl stopper (Datwyler)

- Both suppliers have performed additional testing to support the coring performance claims under actual usage conditions (i.e. 20 piercings)

Coring and self-sealing testing protocol (adapted from EuPharm)

Number of stoppers tested: 12 (gamma irradiated)

- Needle: 23G
  Rationale: On a general basis, 23G to 25G needles are used in liquid vaccines and notably intramuscular injection. 23G needles may be considered as a worst case due to a larger diameter

Number of piercings per vial: 20

Test results:

- Number of fragments detected after 20 piercings: Zero
- Self-sealing test after 20 piercings: Pass

Survey Responses: 10R & 20R Glass vials

- Interest expressed for both 10R & 20R vials

Question	# of Responses
10R Vials	6
20R Vials	4
Not Interested	5

Survey Responses: Estimated number of Glass vials

- All responses are shown in the table below

Response	# of 10R Glass Vials (M)	# of 20R Glass Vials (M)
		Max. avail.
	Up to 30	
		20
	25	
	15-42	
	10	
Totals	55	20

Overall total = 100 – 127 M for 10R & 20R combined

Note: Names of companies omitted for confidentiality

Survey Responses: Interest in DP Network

- 73% of respondents indicated an interest in participating
- Majority have interest in aspects of the DP Network, particularly glass vials and Fill/Finish capacity

Interest in DP Network	# of Responses
Yes	11
No	4

Access to which aspect of DP Network	# of Responses
Glass Vials	9
Fill/Finish capacity	9
Novel/alternative preparations	5
Not interested in the DP Network	4

Questions for today

- Do you have any questions/concerns about the vial supplies from OMPI? Italy? Mexico?

- Do you have any questions/concerns about stoppers from Aptar or Datwyler?

- Confirm preference for 10R vs 20R
  - Verify quantities of 10R or 20R vials you will need from CEPI supplies?

- On tops of the vials, do you want access to any of the following items from CEPI for your product:
  - Stoppers
  - Aluminum caps
  - Vial adapter

Questions for today

- Have you already started some stability/container compatibility studies on your product?

- Do you need to receive samples of the vials/stoppers/caps (how many/timelines)?

NEXT STEPS: Organize one-to-one (Developers/CEPI sustainable manufacturing team) meetings to secure access to vials/stoppers/caps

Break

Drug Product Network Design

Key strategic considerations

- Strategic and technical rationale for the project
  - *Objective was to perform selection of DP Sites in order to be ready for DP manufacturing in September/October 2020*
  - *Scope included all vaccine Modalities, sufficient capacity for 4 Bn doses, all geographies*
- Fit with overall COVAX R&D&M objectives
  - *This project is a critical element for the successful manufacturing and delivery of the COVID-19 vaccines under development*
- Critical milestones and timing
  - *Receive Interest and Commitment from Vaccine Developers (3 August 2020)*
  - *Decide on primary packaging components (3 August 2020)*
  - *Reserve Capacities (31 August 2020)*
  - *Decide on Criteria to Start Tech Transfers (31 August 2020)*
- Critical risks
  - *It is unknown today which vaccines will be successful and for which ones we will do the tech transfers and manufacturing*
  - *We plan to perform tech transfers and manufacturing at risk on the basis of positive signals from clinical trials*

CEPI’s DP strategy

- Developed a global DP strategy
- Setting up a DP Network for 2 to 4BN doses of 2-3 COVID-19 vaccines (9 in portfolio)
- Access to this network is open to all vaccine developers intending to participate in the COVAX Facility regardless of whether they are a recipient of funding from CEPI or the foundation
- Network attributes:
  - Able to manufacture all vaccine modalities (RNA, pDNA, recombinant protein, viral vectors, adjuvants, diluents)
  - Able to produce DP starting Sep/Oct 2020
  - Be established around the globe
  - Fill multidose vials
- CEPI will set up the network, so vaccine developers can leverage the network capabilities

Key characteristics of the DP network

DP Site Selection Process

- CEPI, together with BMGF and CHAI, conducted a survey of over 200 companies, institutions and CMOs of available DP capacity
- CEPI shortlisted 23 companies which were then interviewed using a structured interview process
- CEPI has selected companies with appropriate Quality and Regulatory Track Record and geographical distribution to supply vaccines in 2020 and 2021 (and beyond)
- **DP Sites**
- CMOs and/or Pharmaceutical companies, global footprint
- Will be able to process RNA, DNA recombinant proteins, live viral vectors and adjuvants
- Will cover formulation, filling, visual inspection, labelling, packaging, analytical testing and QA release
- Are able to allocate sufficient capacity to the manufacturing of COVID-19 vaccines in 2020 and 2021
- Have a good Quality and Regulatory Status

Capacities

- In 2020, the selected sites can fill more than 400 M doses in vials
- In 2021, the selected sites can fill more than 4 BN doses in vials (could be expanded if needed)
- If more capacities are required, CEPI can expand the network

Raw Materials

- DP Network will have access to glass vials, rubber stoppers and crimp caps that have been reserved by CEPI

Regulatory

- The network sites will preferably be approved by major health authorities and/or have WHO/PQ
- WHO is considering an EUL process for sites which do not yet have WHO/PQ

Contractual and network management considerations

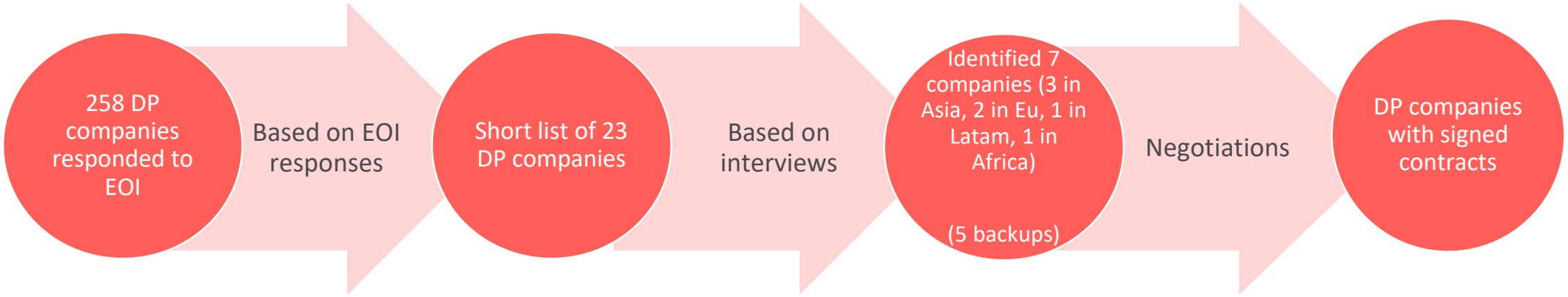
Capacity Reservations / Contracting

- CEPI will reserve capacities at the DP Sites
- The Capacity reservations will depend on the Interest and Commitment of the Vaccine Developers
- Final Answers would be needed on August 3rd
- CEPI will agree with DP Companies on Key Contractual Terms
- Vaccine Developers can then contract with the DP Companies under these conditions and at reduced risk (if their vaccine fails)
- Sufficient capacities for vials, stoppers etc., can also be secured by CEPI at attractive conditions
- If we are reserving the capacities for the vaccine portfolio, the risk of “unused capacity” is going to be reduced

Network Management

- The global vaccine manufacturing and distribution efforts will require excellent coordination of all steps in the Supply Chain
  - Procurement and logistics for vials, stoppers, caps, labels, cartons, etc.
  - Tracking materials through supply chain, including through release at CMO, by development partner, and NRAs
  - Global coordination of logistics
- Vaccine Developers will be responsible for product quality and release; quality agreements with DP network partners.
- CEPI is in touch with several Multinational Companies which expressed willingness to support these global coordination efforts

Process of selection for DP network building



- 258 DP companies had responded to EOI survey
- Shortlisting based on DP Strategy criteria

- 23 short listed companies were invited to interviews, all responded and were interviewed
- Filter based on
  - Capacity of >100M/year
  - Regulatory approval by SRA and/or WHO-PQ of at least one product
  - High throughput of manufacturing

- Aligned with WHO on selection
- Initiated contract negotiations with 7 DP companies
- Get Buy-in from Vaccine Developers
- Perform On-Site Due Diligences

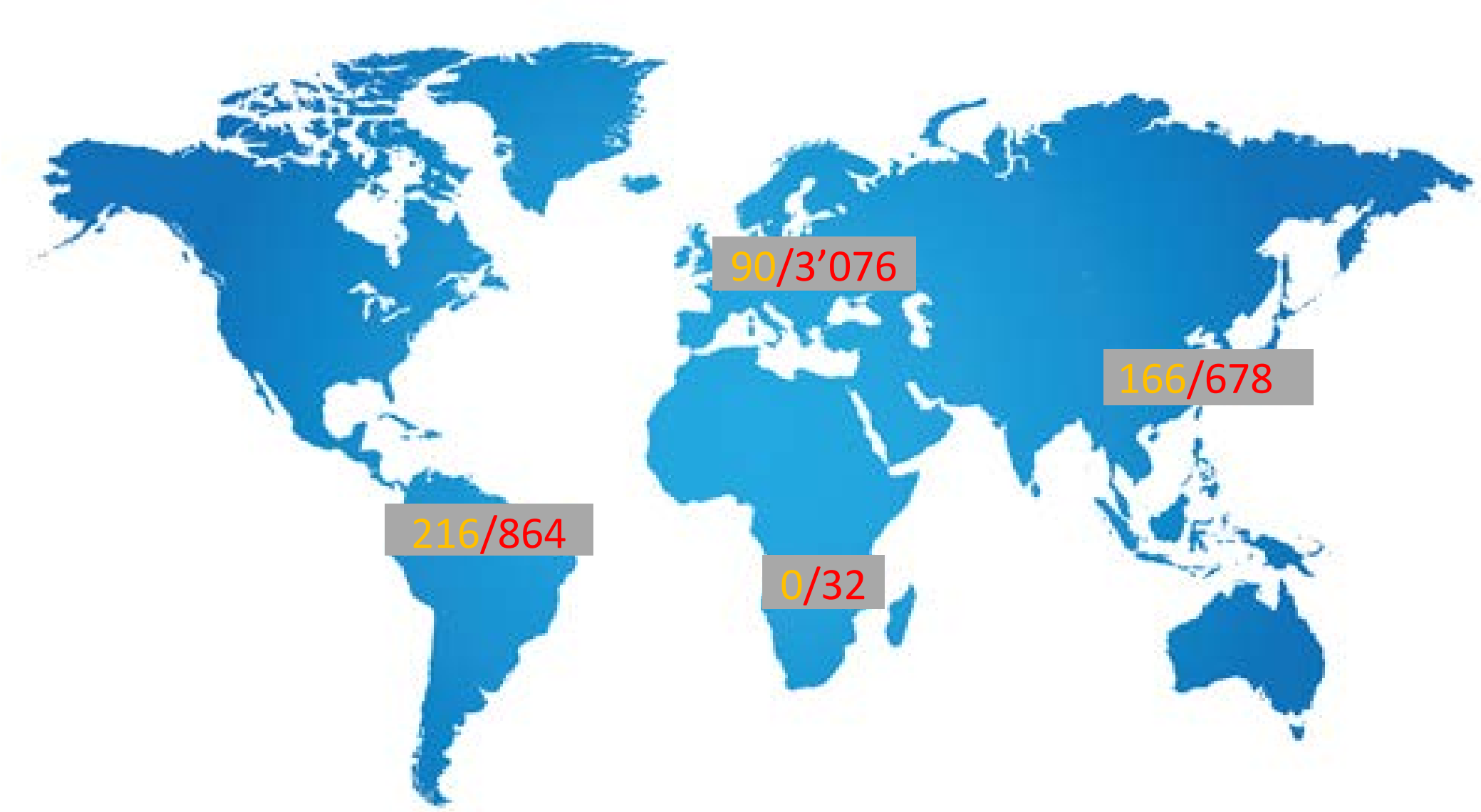
Interview and Selection Process

- Development of Interview Guide based on DP Strategy (90 questions)
- Performance of structured interviews, also providing info to DP Companies
- Scoring and Selection based on assessments of “Must Have” Criteria and “Desirable Criteria”, per geography

Resulting Capacities of seven selected DP Companies
(in Million Doses in 20R Vials)

	2020	2021
• Europe 1	90	2’700
• Europe 2	0	376
• Asia 1	30	150
• Asia 2	106	353
• Asia 2	30	175
• Americas 1	216	864
• Africa 1	0	32
• **Total**	**472**	**4’650**

Geographical distribution of capacities 2020/2021



Project Risks

Risk Assessment

Risk	Mitigation
• Tech Transfers is initiated too early in product development	➢ Develop clear criteria for Tech Transfer Decision
• DP Sites may not deliver all doses committed	➢ Reserve capacity for > 2BN doses (so that 2 BN vials will be available, despite potential attrition)
• Some Countries may not allow exportation	➢ Reserve capacity for >2BN doses in multiple geographies; have clear agreements with governments
• Local COVID-19 outbreaks may hinder manufacturing	➢ Reserve capacity for >2BN doses in multiple geographies
• Transportation breakdown & supply chain disruptions due to COVID-19	➢ Reserve capacity in multiple geographies
• Reserved Capacities may not be fully used	➢ Reservations are for portfolio vaccines, get commitments from vaccine developers

Summary and Next Steps

Survey Responses: Interest in DP Network

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Not interested in the DP Network	4

Summary

DP Sites

- CEPI has carefully selected seven DP sites, with high capacity, good quality track record and good geographical distribution
- The sites are able to process RNA, DNA recombinant proteins, live viral vectors and adjuvants
- Will cover formulation, filling, visual inspection, labelling, packaging, analytical testing and QA release
- If more capacities are required, CEPI can expand the network

Contracting

- Based on Interest of Vaccine Developers, CEPI will reserve capacities at the seven sites
- Vaccine Developers will sign their own Service and Quality Agreements with the DP Sites
- If required, a Network Management Company can be hired in order to support with Supply Chain planning, logistics etc.

Raw Materials

- DP Network will have access to glass vials, rubber stoppers and crimp caps that have been reserved by CEPI, but this is not a requirement

Timelines and Proposed Key Next Steps

Until August 3rd 2020:

- Get feedback from partners on DP interest as well as primary packaging components

ASAP:

- Provide DP companies with vials, stoppers and crimp caps for machinability tests
- Need to have fixed vial decision for this

Until August 31st 2020:

- Reserve Capacities at selected Companies, develop key elements of MSAs in parallel
- Sign LOIs with backup companies which are currently booked by bilateral agreements
- Decide on Criteria to start Tech Transfers

Until Sep 30th 2020:

- Over next 8 weeks: Perform On-site Due Diligences at the selected companies, starting with the Tier 1A companies

Partner Interest in our Drug Product Network

- What remaining questions are there regarding the use of the network?
- Do you confirm interest in using the network?
- What conditions would be important for partners to join the network?

NEXT STEPS: Organize one-to-one (Developers/CEPI sustainable manufacturing team) meetings to discuss conditions to use the network

Back up Material

Proposed Deployment Approach in Phases

	2020	2021
• Europe 1	Mfg	Mfg
• Europe 2	TT	Mfg
• Asia 1	TT	Mfg
• Asia 2	Mfg	Mfg
• Asia 3	TT	Mfg
• Americas 1	Mfg	Mfg
• Africa 1	TT	Mfg

Live Virus Vaccine Capacities

	2020	**2021**
• Europe 1	90	2’700
• Asia 3	30	175
• Americas 1	216	864
• **Total**	**336**	**3’739**

AOB