Expression of Interest on supply of COVID-19 vaccines on behalf of the COVAX Facility

Public version, 31 August 2020

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Expression of Interest (EOI) overview

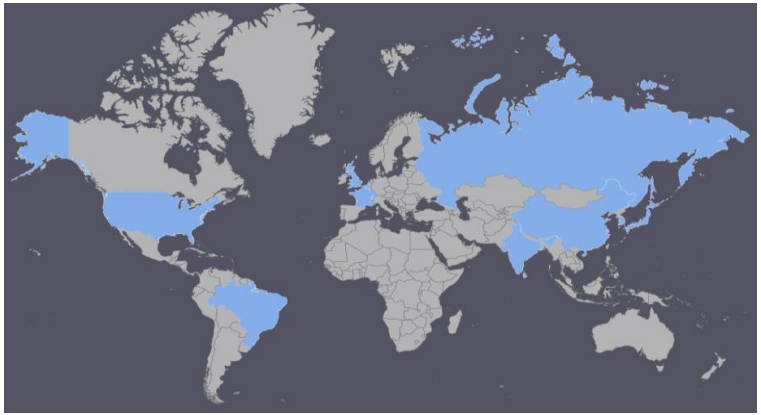
- UNICEF issued an EOI on 15 June 2020 on behalf of the COVAX Facility
- EOI Objectives: **Understand manufacturing plans** and **help inform design elements of the COVAX Facility** and the associated procurement approach
- Vaccine developers and manufacturers were invited to provide information on a range of topics (listed below). Data were compiled as of 1 July 2020.
- COVID-19 vaccine information requested:
  - Production volumes
  - Manufacturing platforms
  - Timing of availability
  - Product presentation
  - Pricing policy (e.g. 'flat' price for all countries, tiered pricing,…)
  - Support needed (e.g. on licensure pathway, registration…)

Respondents to the EOI

In alphabetical order:

Anhui Zhifei Longcom Biopharmaceuticals	NingBo RongAn Biological Medicine
AstraZeneca	Novavax
Aurobindo Pharma Ltd	Panacea Biotec
Beijing Institute of Biological Products	Pfizer
Beijing Minhai Biotechnology Co.	Sanofi Pasteur
Bharat Biotech International Limited	Serum Institute of India (SII)
Biological E Limited (BioE)	Shionogi & Co.
Chengdu Institute of Biological Products	SinoCellTech
Chumakov	Sinovac
FSUE	SK Biopharmaceuticals
GSK	StemiRNA Therapeutics
Indian Immunologicals Ltd	Takeda
Janssen	Walvax Biotechnology Co.
Merck MSD	Wuhan Institute of Biological Products

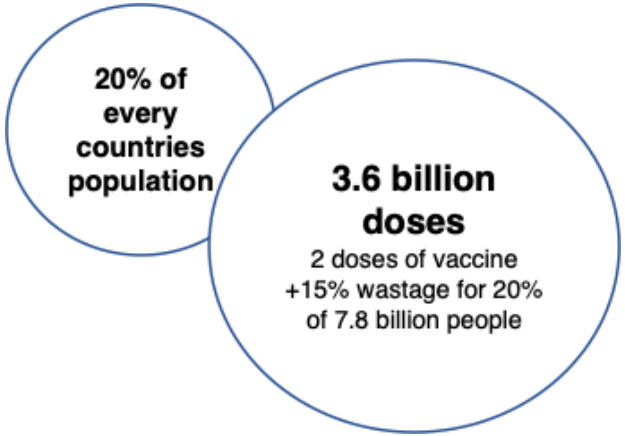
- 10 with manufacturing in China
- 6… in India
- 3… in the USA
- 2… in each of Belgium, Russia, Japan
- 1… in each of France, S. Korea, Switzerland and the UK



Demand and Supply (i.e. aggregated production capacity estimates from manufacturers)

How much vaccine is needed globally?

- Global vaccine demand depends **on how long immunity lasts, the effectiveness of the vaccine & the number of doses per vaccine course** (assumption is 2 doses per course)
- **The ACT-A goal is to secure "2 billion doses by 2021"**
- **WHO is developing a framework to allocate COVID-19 vaccines. The current draft allocates as follows:**
  - Every country receives doses for 3% of their population to reach health and social care workers with an immunisation course
  - Then, every country receives second allocation for up to 20% of their population to reach people over the age of 65 and people at higher risk of critical Covid-19 disease due to underlying conditions
  - Combined, these amounts exceed the 2 billion dose target for ACT if we assume they are needed prior to end 2021. The higher of the two volumes was used.



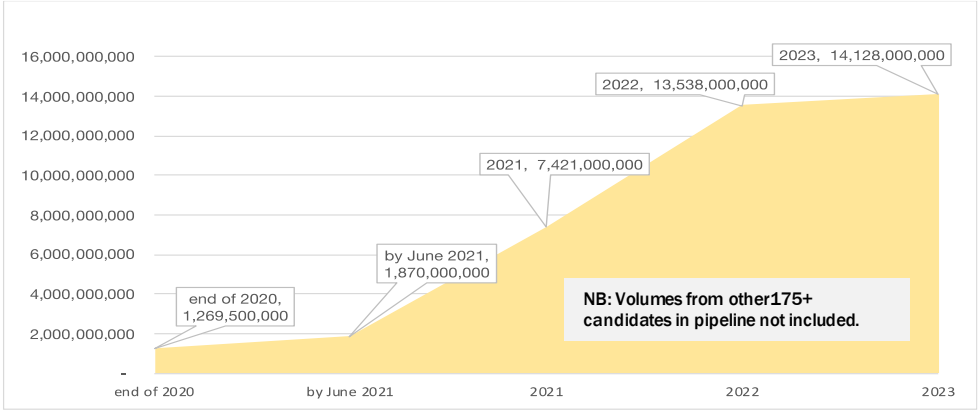
How much vaccine might be available?

Global aggregate supply volumes compared with global demand scenario

Aggregate Supply Volumes

Number of doses, as indicated in EOI or publicly stated (NB: Data unqualified)

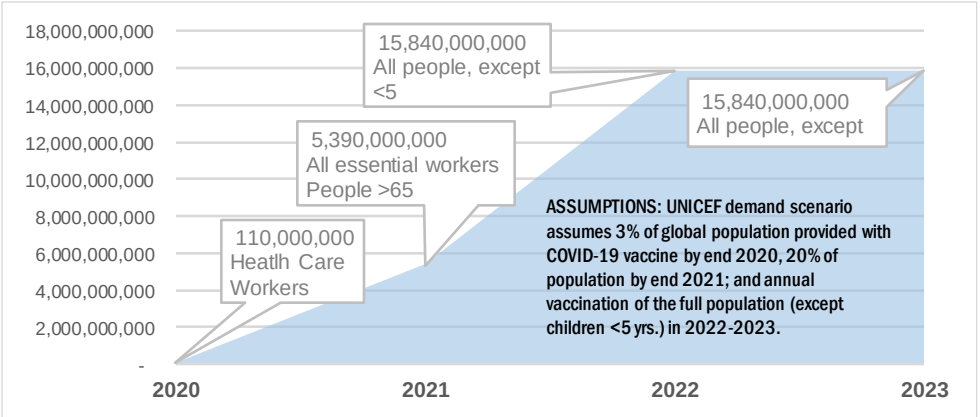
By end 2020: 1.3 billion
By June 2021: 1.8 billion
By end 2021: 7.4 billion
By end 2022: 13.5 billion
By end 2023: 14.1 billion



UNICEF Demand Scenario

Global demand scenario, annual vaccination

By end 2020: 110 million
By end 2021: 5.4 billion
By end 2022: 15.8 billion
By end 2023: 15.8 billion



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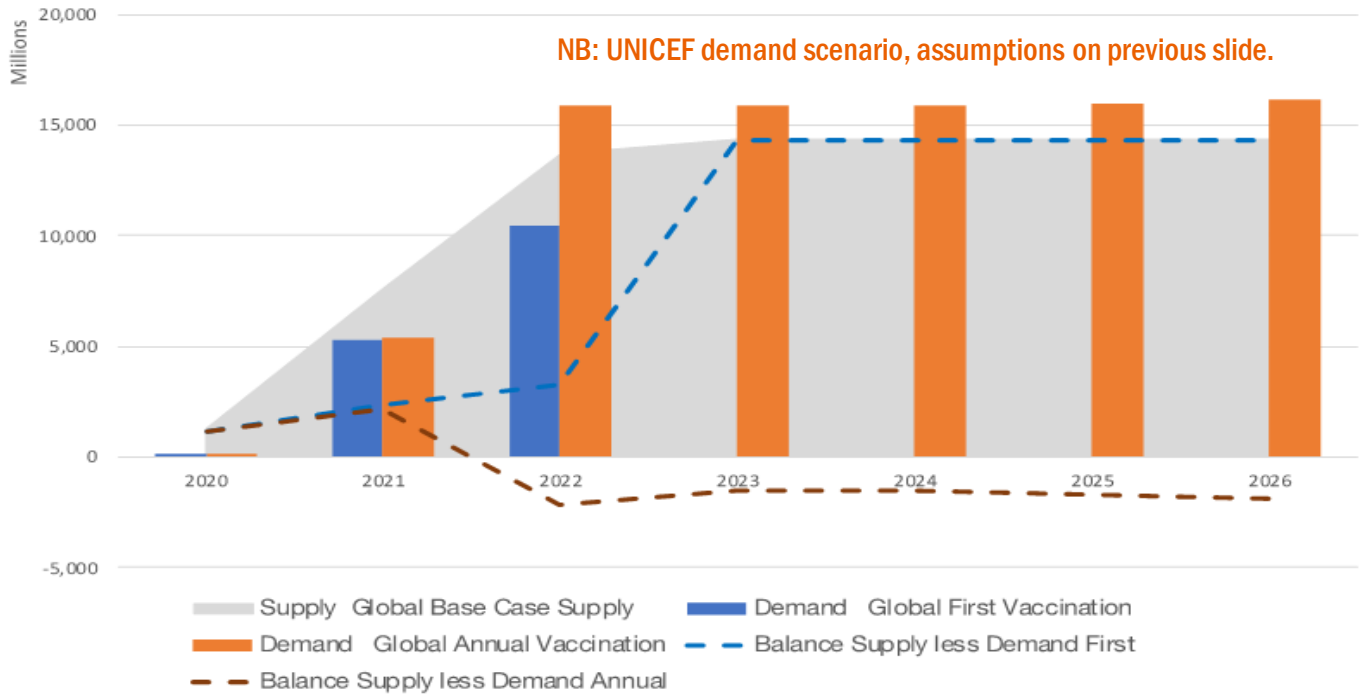
Global aggregate supply vs. demand projection

Planned production in 2020-2021 will be tight compared to aspirational demand.



Considerations

(How to interpret global supply volumes)

- Supply (i.e. production capacity estimates) from individual manufacturers are self reported .
- No validation has been conducted of manufacturers' production estimates presented here (e.g. through assessment of manufacturing processes …).
- Since EOI was conducted on behalf of COVAX Facility, manufacturers responded with (some) understanding of the Facility and the potential incentives that it offers. This may have influenced responses. For example, we assume projected volumes might have been considerably lower in the absence of the Facility.
- At the time of the EOI, many manufacturers did not know definitively :
  - their production yields at scale (*NB: This will only become apparent once they scale up their production facilities*)
  - the quantity of antigen per dose needed for each vial (*NB: This will only be known following Phase 3 trial completion and regulatory approvals*)
- Global aggregate supply volumes presented here consolidate manufacturer-specific production estimates. No attrition rate (e.g. to predict the proportion of candidates that might not achieve licensure) have been applied.
  - *NB: Historically, success rates of candidates are ~7% in preclinical stages, and ~20% in clinical stages (i.e. 80% to 90% fail). By contrast, the COVAX Facility is assuming a success rate of 50% for its portfolio given that the Facility has prioritized candidates based on scientific feasibility and ability to scale quickly.*
- In instances where manufacturers did not provide an estimate of production capacity in their EOI response, if manufacturers had publicly announced planned production volumes (e.g. as part of a bilateral deal press release), these estimates were used to (partially) fill data gaps. In other instances, where manufacturers did not provide an estimate and none could be found in the public domain, no production volumes were assumed for the individual manufacturer.

Different lenses on aggregate production capacity estimates

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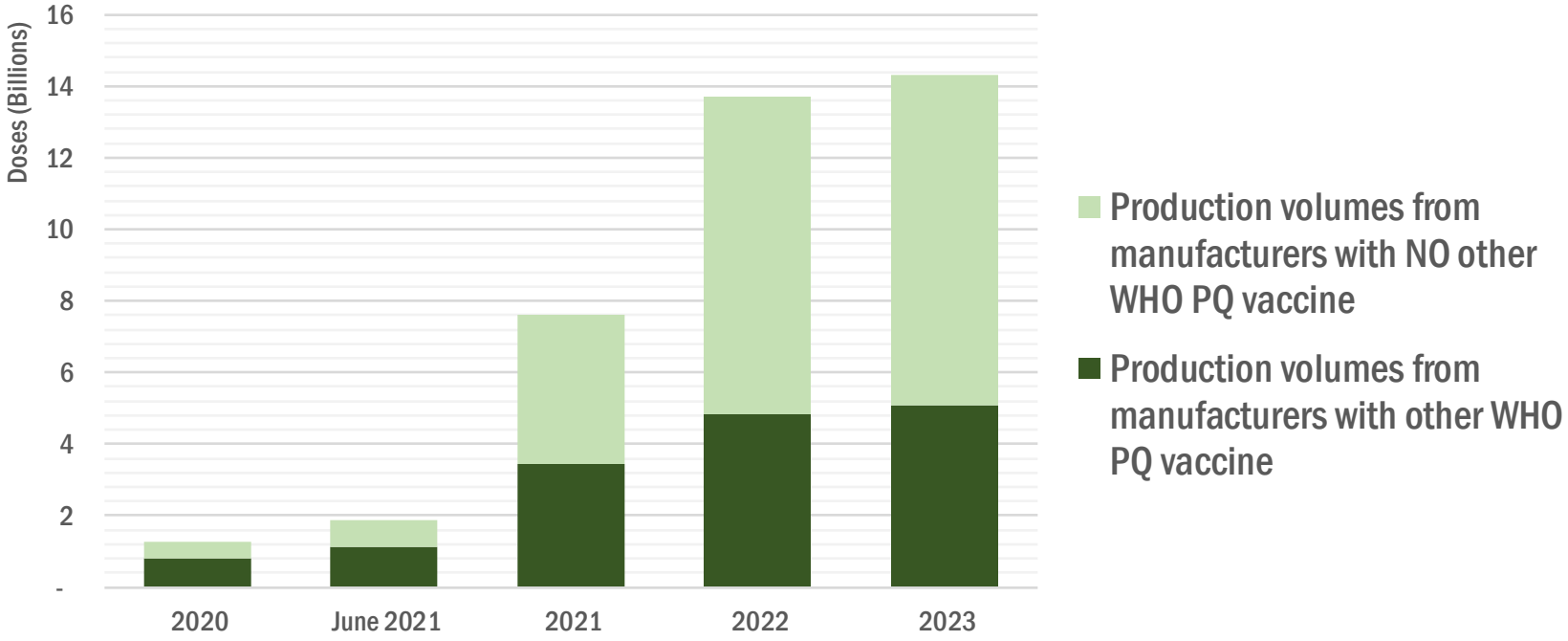
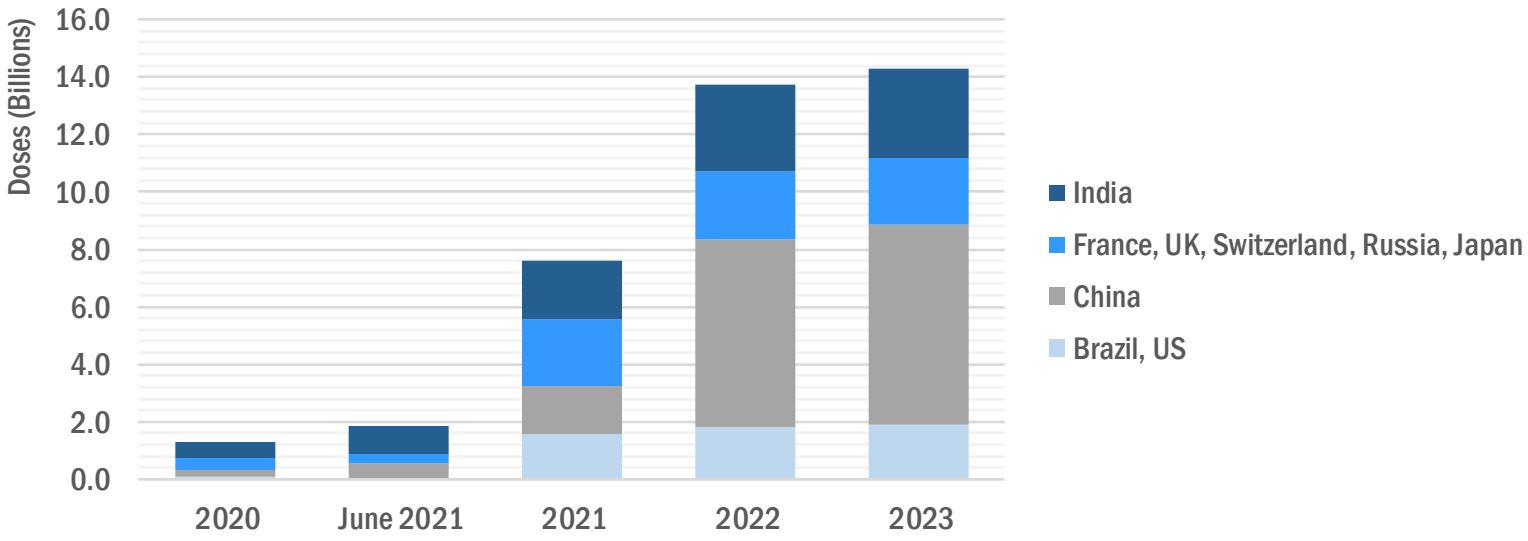
Indicated annual production volumes from manufacturers with another WHO prequalified vaccine vs. those without a prequalified vaccine

Potential high dependency on manufacturers that have never taken a vaccine through WHO prequalification (PQ)



Indicated annual production volumes by location of manufacturing

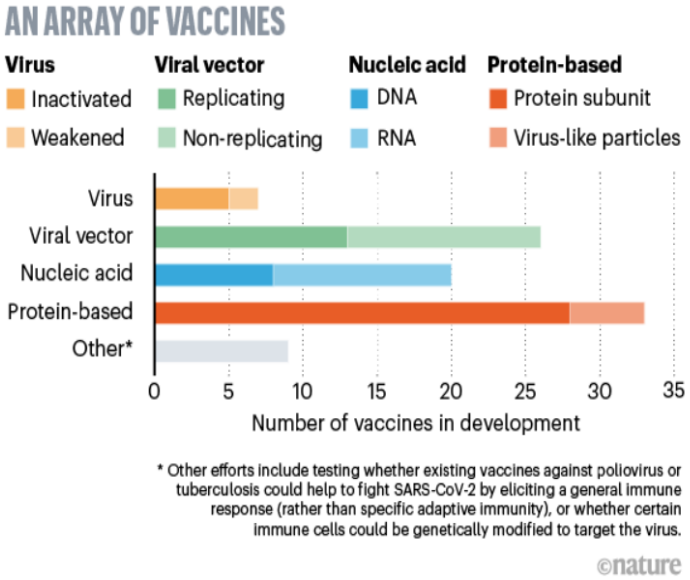
Reliance on manufacturers whose production is located in one of nine countries



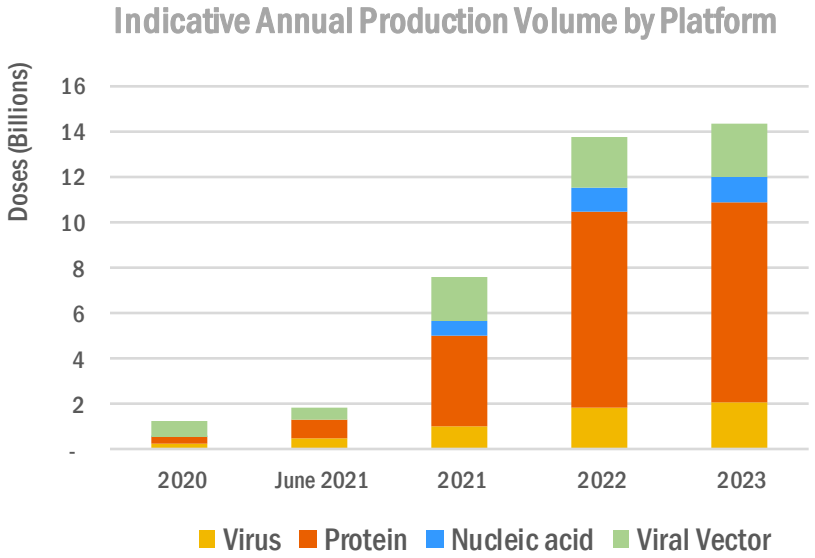
- In 2020, 19% are from mfrs in China; 22% are from mfrs in India
- In 2023, 49% are from China; 22% from India

Vaccine platform

In 2020/2021, volumes spread across platforms. By 2022/2023, protein-based candidates account for majority of volumes indicated across manufacturers



Sources: *Nature* analysis based on: WHO COVID-19 Vaccine Landscape/Milken Institute COVID-19 Treatment and Vaccine Tracker/T. Thanh Le *et al. Nature Rev. Drug. Disc.* http://doi.org/ggrnbr (2020)/F. Amanat & F. Krammer *Immunity* **52**, 583–589 (2020)/W. Shang *et al. npj Vaccines* **5**, 18 (2020).



Source: UNICEF COVID-19 Vaccine EOI, June 2020 and manufacturer-specific data available in the public domain. NB: This chart does not distinguish between sub-classes of platforms (e.g. Replicating and Non-replicating Viral vector candidates are listed together under 'Viral Vector' platform).

Vaccine platforms have different risks and pace

Platform and considerations	Global aggregate supply volumes indicated, 2020-23	Manufacturers indicating platform and production volumes*
Virus: Weakened or inactivated. Often requires more safety testing. Majority of current vaccines (Vx).	5.7 billion 15%	Beijing Biom., Beijing Inst., Bharat, Chumakov, Indian Imm., Panacea, Sinovac, Wuhan
Viral vector: Modified. Safer. NB: While an rVSV-ZEBOV (Ebola vaccine) is licensed, and is a replicating viral vector Vx, no *non-replicating* Vx has been licensed.	7.7 billion 20%	AstraZeneca, Aurobindo, Bharat, Chengdu, Fiocruz, Janssen, Shionogi, SII, Walvax
Nucleic acid: Expected to be easier to develop and manufacture, but no RNA or DNA Vx has been licensed.	2.8 billion 7%	Inovio, Moderna, Pfizer, StemiRNA, Walvax
Protein-based: Require adjuvants and multiple doses. Can be hard to manufacture.	22.5 billion 58%	Anhui, BioE, Novavax, Sanofi, SinoCellTech, Walvax

*Indications come from a mixture of EOI responses and information available in the public domain

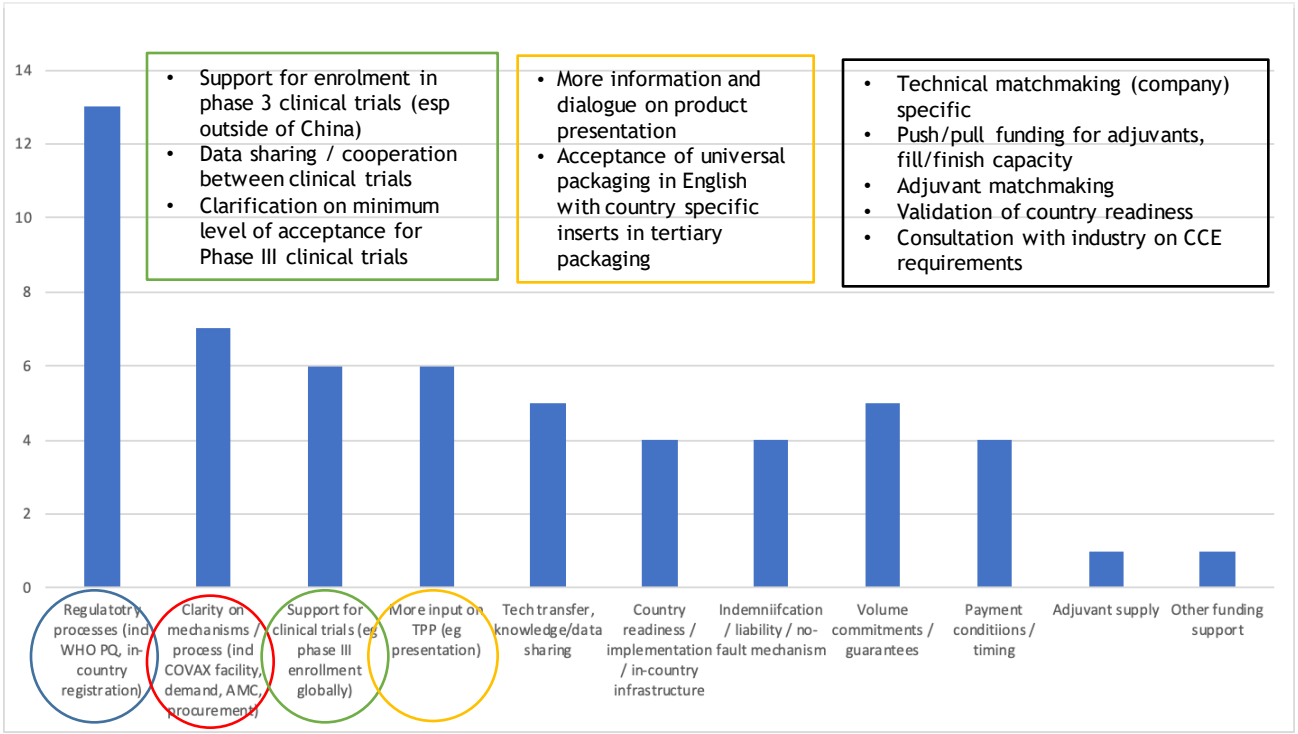
Additional needs and possible supply chain risks/considerations

Risks identified and support/information requested by manufacturers

Regulatory pathway, country licensing, indemnity, clinical trials, COVAX Facility design

- Streamlining / harmonizing regulatory processes at national and global level
- Accelerated PQ process (ref lessons learned from Ebola)
- Creation of an emergency use pathway
- Support to in-country registration

- Consultation with industry on mechanisms & processes
- Information on what type of support is available to manufacturers & when
- Communication & consultation with industry on demand, programmatic policy & approaches



- Support for enrolment in phase 3 clinical trials (esp outside of China)
- Data sharing / cooperation between clinical trials
- Clarification on minimum level of acceptance for Phase III clinical trials

- More information and dialogue on product presentation
- Acceptance of universal packaging in English with country specific inserts in tertiary packaging

- Technical matchmaking (company) specific
- Push/pull funding for adjuvants, fill/finish capacity
- Adjuvant matchmaking
- Validation of country readiness
- Consultation with industry on CCE requirements

Vaccine specifications

[NB: Most information just indicative]

- All **liquid** except some **freeze-dried** products
  (*NB: Freeze dried can be more stable but require another manufacturing step; i.e. slower to scale; and more room for administration error*)
- All indicated **intramuscular injection**, except one nasal atomisation
- Majority indicated **2-dose course**, a few indicated single dose, one indicated single dose with booster, one indicated 3-dose course
- Majority indicated vaccine would be provided in a **multi-dose vial**
  - Number of doses per via to be decided (8)
  - >50 doses per container (2)
  - A plan for vial size - 1, 2, 5 or 10 (6)
  - Pre-filled syringe (5)
- Most have target temperature requirement of stability between 2°C and 8°C.

  ➢ But thermostability data takes time … **so could expect ultra cold chain (-60°C) temperature requirements or freezing (-20°C)** and shorter shelf life during 2020-2021

Reflections and key messages

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Will a COVID-19 vaccine be a silver bullet?

- Indications of global vaccine production is positive.
- The impact of a vaccine depends on **how long immunity lasts, the effectiveness of the vaccine, and changes in the virus and underlying epidemiology**
- Likely to be different vaccines with different efficacy, different durations of protection, different and presentations, different suitability in different contexts
- Short duration and modest effectiveness may imply a need for **booster vaccination or annual vaccination.** This will have a marked impact of supply sufficiency.
- **Limited availability of doses compared to demand in initial year(s)** means COVAX Facility is focused on protecting public health (e.g. vaccinating health and social care workers) and minimizing COVID-19 mortality (e.g. vaccinating elderly populations and those with comorbidities). This implies that COVAX Facility, and vaccines in initial years will not be sufficient to eliminate the virus.

"The durability of immunity [to common coronaviruses] *that is protective, ranges from 3 to 6 months to almost always less than 1 year"*
Director, NIAD, Anthony Fauci

50% efficacious:
WHO and FDA minimum acceptable standard for COVID-19 vaccines

Key Messages

- **The aggregate supply situation could not be more optimistic with manufacturers planning massive and accelerated scale up of COVID-19 vaccine production** despite the fact that production volumes were not indicated by some EOI respondents
- **Unprecedented rapid pursuit for development and production scale-up** of COVID-19 vaccines, reducing what would normally take 10+ years to potentially 1-3 years
- **Global COVID-19 vaccine portfolio has a healthy diversity** of platforms, manufacturing locations and partnerships
- **Planned production in 2020-2021 will be tight compared to aspirational demand.** Careful dose allocation will be key to maximise impact (country readiness, basis for allocation, etc.)
- **Reasonable to assume that sufficient vaccine supply will be available for widespread global roll-out starting in late 2022**; but also possible that annual vaccination or booster doses could be needed
- **Manufacturers have signalled a need for support and clear pathways** in variety of areas. Assessment points to supply chain risks and bottlenecks related to:
  - Potential dependency on manufacturers that have never taken a vaccine through WHO prequalification
  - Reliance on manufacturers in a small number of countries
  - Initially limited thermostability data, and hence potential freezer / ultra cold chain storage requirements
  - WHO emergency use listing (especially in the context of large array of platforms)
  - Country licensure and registration requirements
  - Liability and indemnification

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