COVID-19: UPDATE
Vaccines and Variants
GLOBAL EQUITY

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EI

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12 of the leading COVID Vaccines from multiple countries Source: NYTimes "vaccine tracker": https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html

Leading vaccines

Developer	How It Works	Phase	Status
Pfizer-BioNTech	mRNA	2 3	Approved in several countries. Emergency use in U.S., E.U., other countries.
Moderna	mRNA	3	Approved in Switzerland. Emergency use in U.S., U.K., E.U., others.
Gamaleya	Ad26, Ad5	3	Early use in Russia. Emergency use in other countries.
Oxford-AstraZeneca	ChAdOx1	2 3	Emergency use in U.K., E.U., other countries.
CanSino	Ad5	3	Approved in China. Emergency use in other countries.
Johnson & Johnson	Ad26	3	Emergency use in U.S., Bahrain.
Vector Institute	Protein	3	Early use in Russia.
Novavax	Protein	3	
Sinopharm	Inactivated	3	Approved in China, U.A.E., Bahrain. Emergency use in Egypt, other coutries.
Sinovac	Inactivated	3	Approved in China. Emergency use in Brazil, other countries.
Sinopharm-Wuhan	Inactivated	3	Limited use in China, U.A.E.
Bharat Biotech	Inactivated	3	Emergency use in India.

WHO: SARS-CoV-2 Vaccines and Variants

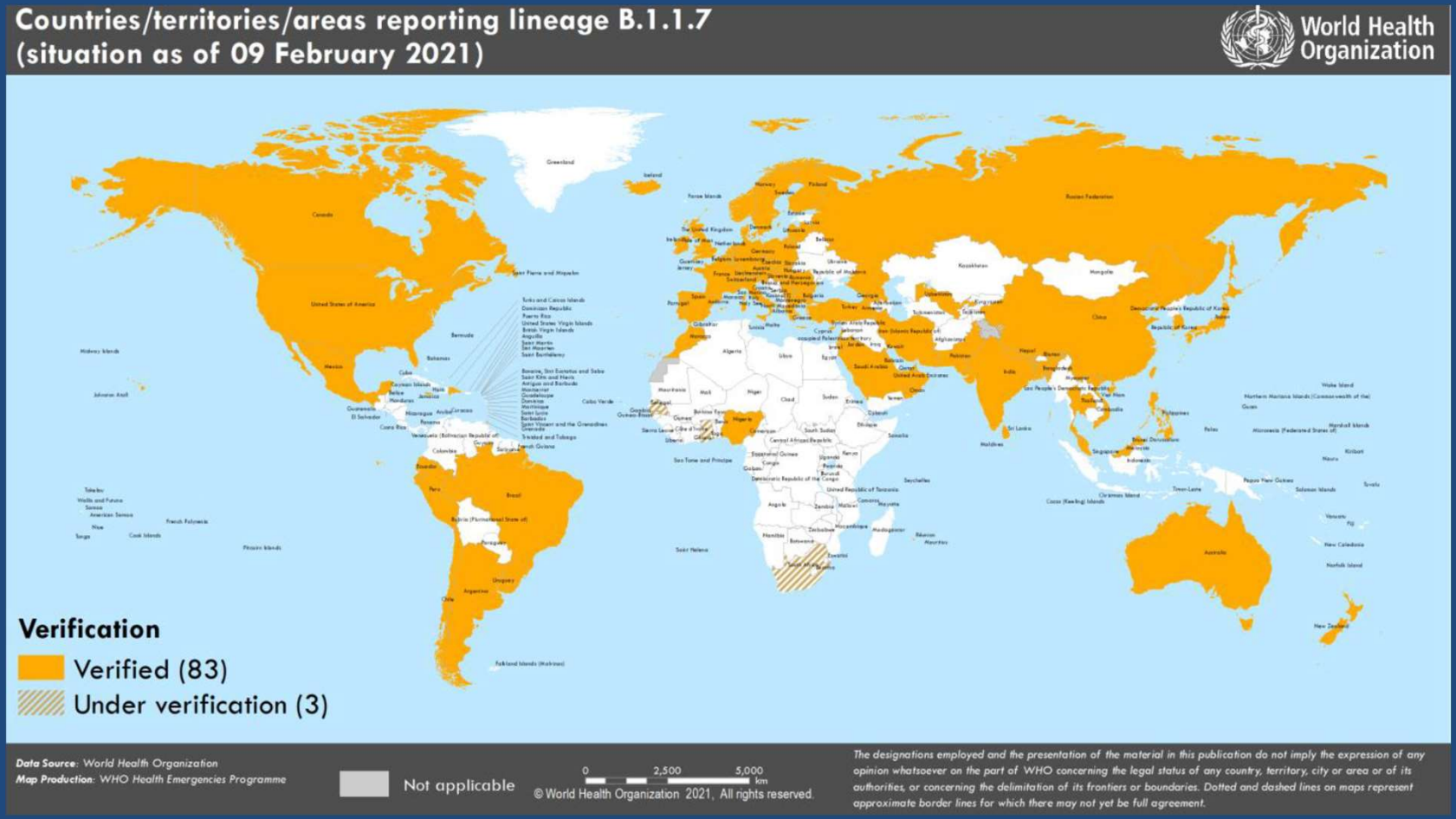
3 Variants of Concern

- Mutations
- Transmission
- Severity
- Impact on Vaccines

- https://www.who.int/publications/m/item/weekly-epidemiological-update---9-february-2021
- https://www.who.int/publications/m/item/weekly-epidemiological-update---10-march-2021

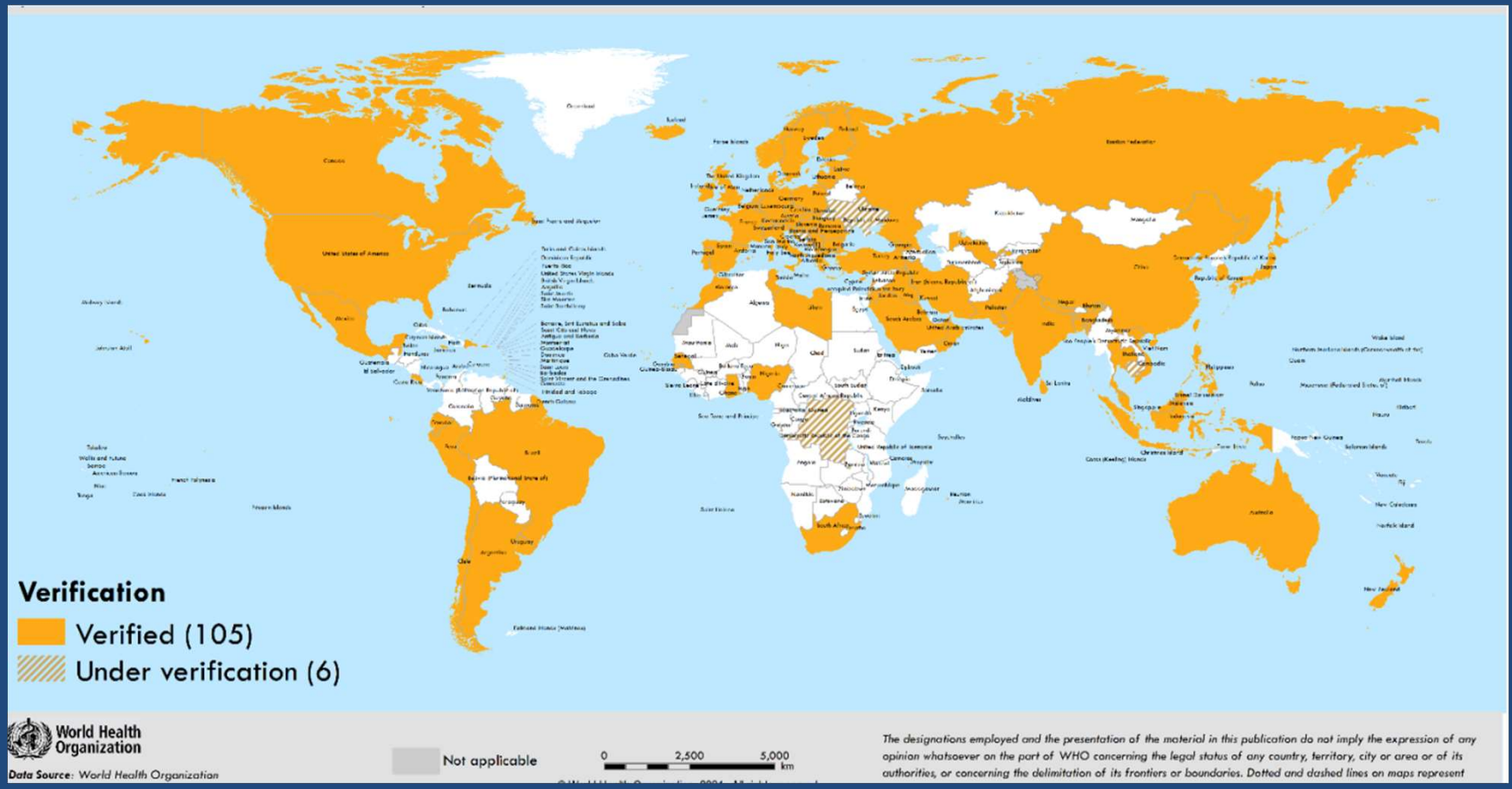
WHO Map of 83 Nations with B117 Variant

https://www.who.int/publications/m/item/weekly-epidemiological-update---9-february-2021



WHO Map of 111 Nations with SARS-CoV-2 VOC 202012/01 B117 Variant

https://www.who.int/publications/m/item/weekly-epidemiological-update---9-march 2021



8 Proposed Criteria for A Template to Assess “Variants”

https://sciencespeaksblog.org/2021/02/02/covid-mega-variant-and-eight-criteria-for-a-template-to-assess-all-variants/

- **More deadly: in adults and/or children**
- **More contagious**
- **Vaccine escape mutants (partial loss of vaccine efficacy to be quantified)**
- Re-Infections are frequent: by epidemiologic and/or virologic evidence
- Monoclonal antibody escape mutants
- Increased risk of “long-COVID”
- Increased risk of Multisystem Inflammatory Syndrome in Children: “MIS-C”
- Antiviral drug resistance

B117 variant

- Transmissibility: Increased (36%-75%)2 , increased secondary attack rate3 (10% to 13%)
- Possible increased risk of hospitalization, severity, mortality
- No significant impact on Moderna, PfizerBioNTech, and OxfordAstraZeneca vaccines
- https://www.who.int/publications/m/item/weekly-epidemiological-update---9-march-2021

WHO Map of 37 Nations with 501Y.V2 Variant

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Figure 6. Countries, territories and areas reporting SARS-CoV-2 variant 501Y.V2 as of 16 February 2021¶

WHO Map of 58 Nations with VOC 202012/02 501Y.V2 Variant

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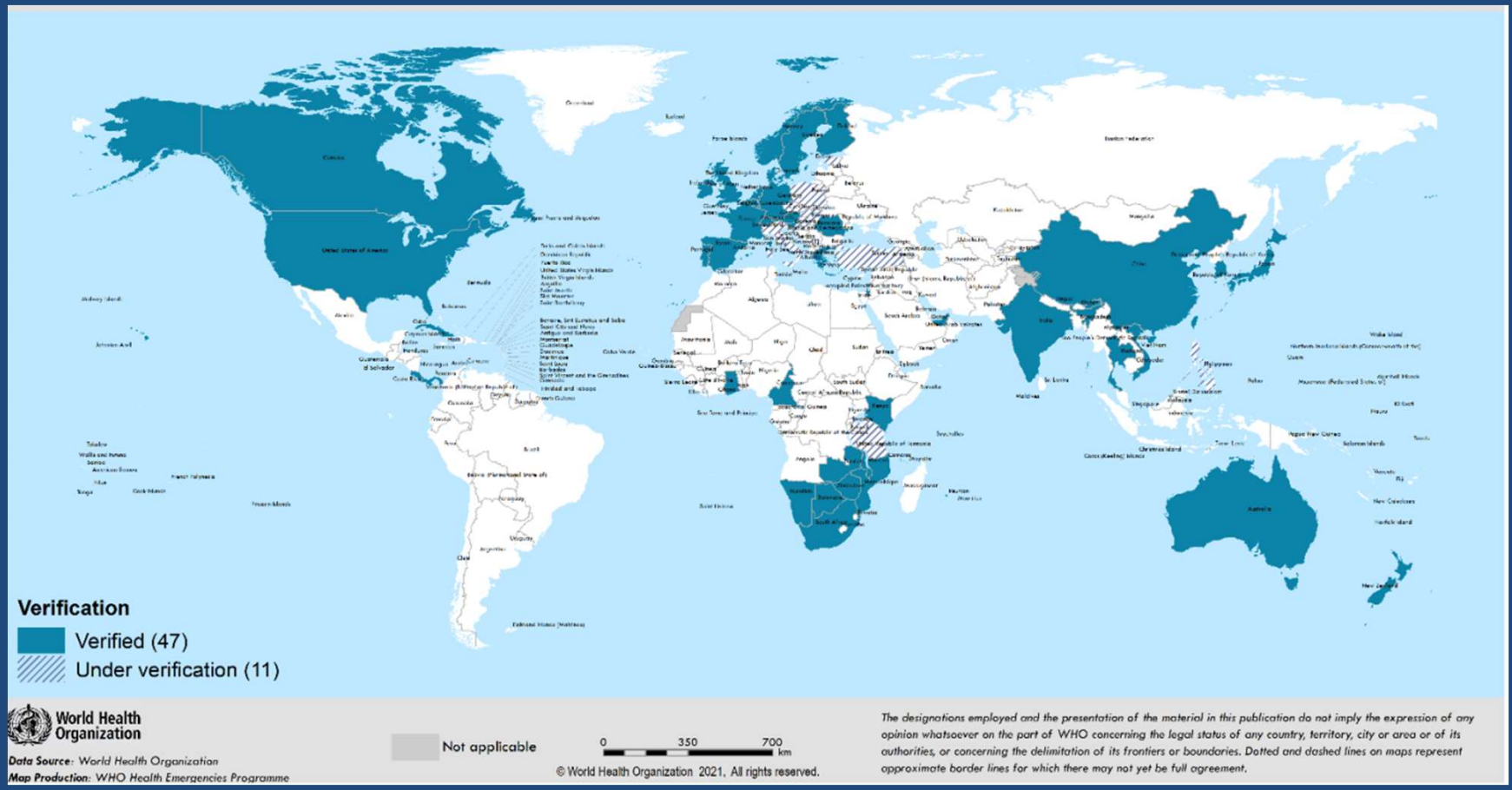
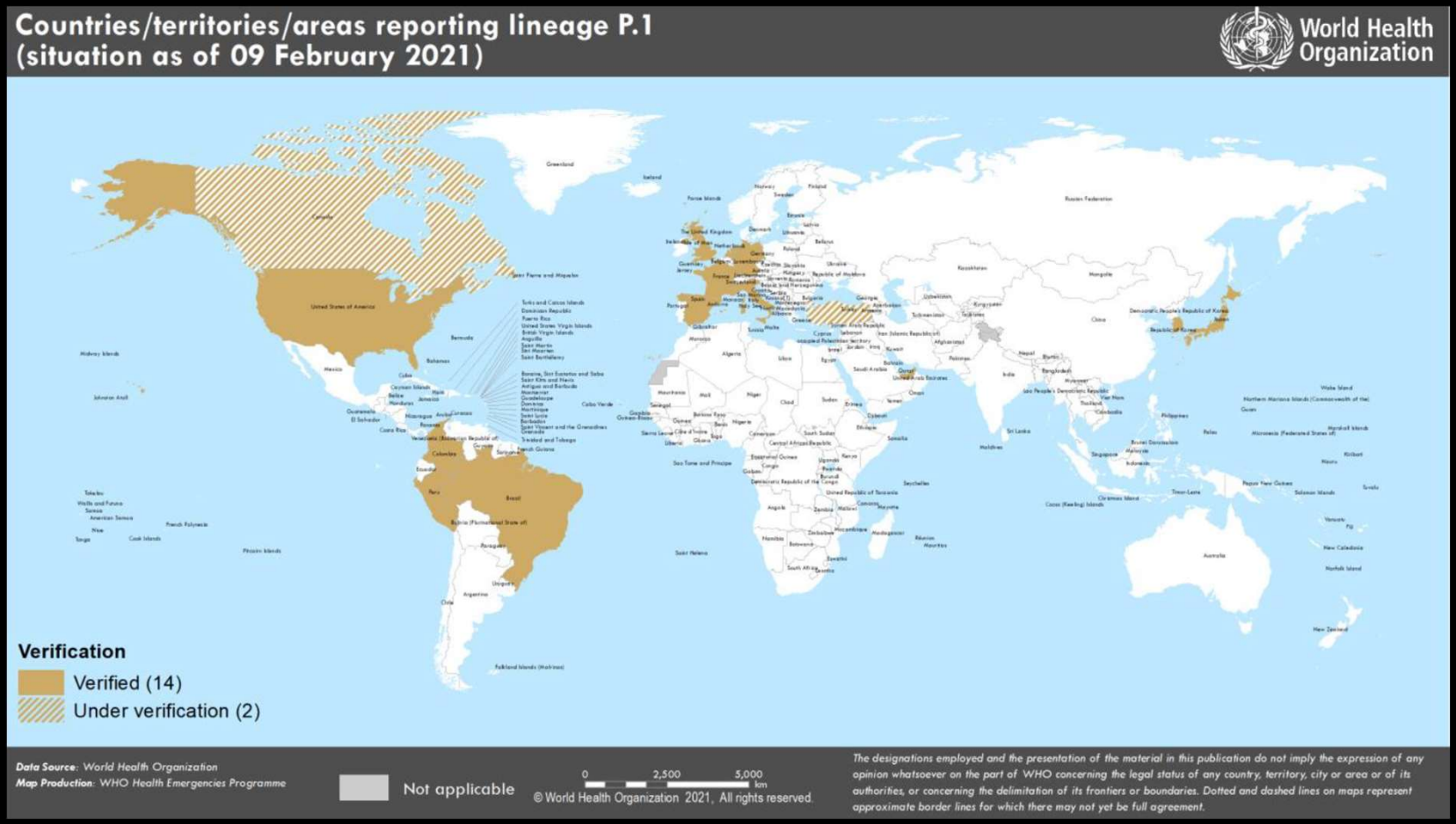


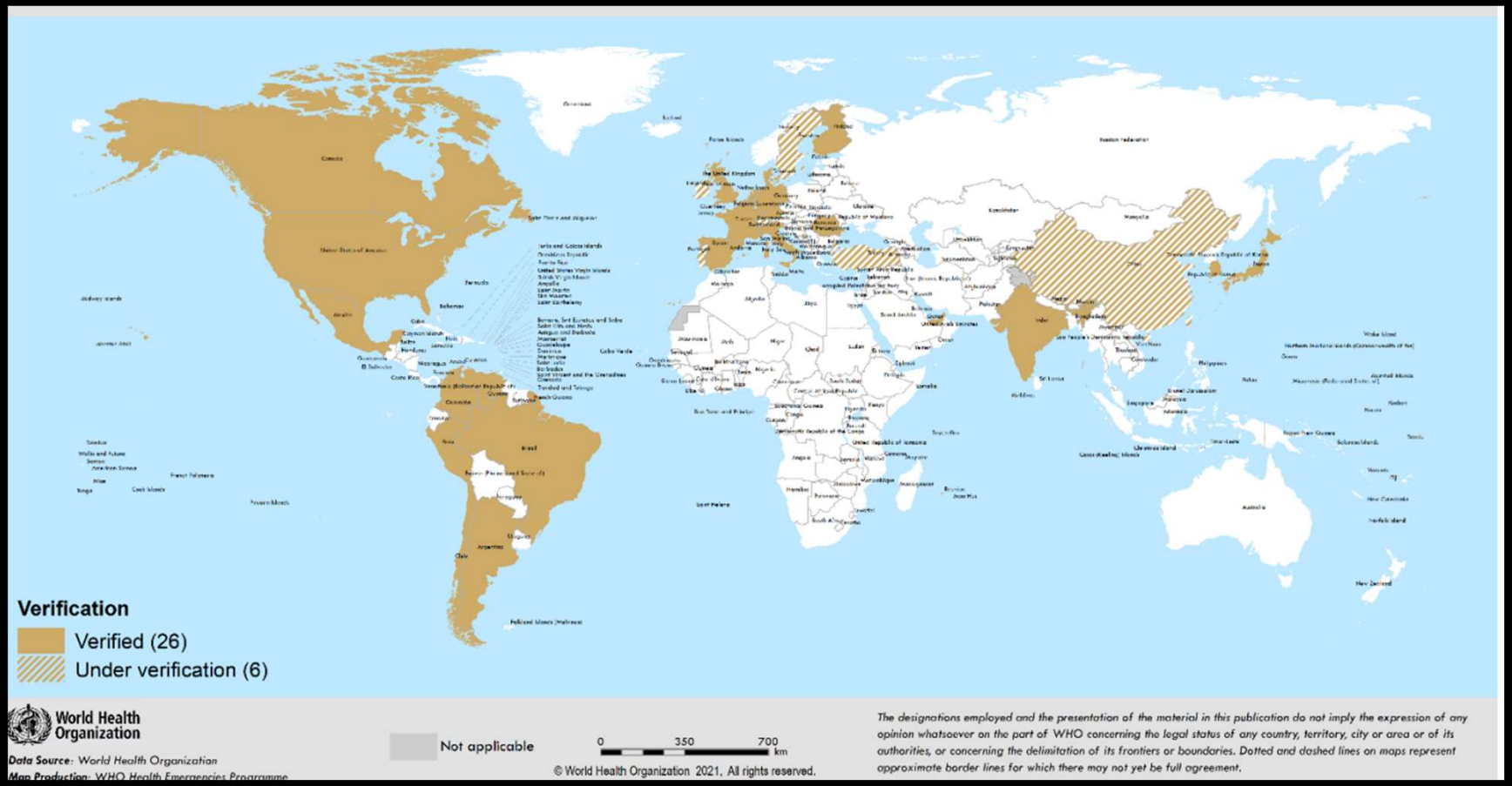
5 Vaccines vs Variant B.351 (501Y.V2)

- Severity: No impact reported to date no significant change in-hospital mortality
- Transmissibility: Increased 1.50 times more transmissible than previously circulating variants
- Moderna and Pfizer-BioNTech: Reduction in the neutralizing activity, but impact on protection against disease not known.
- Novavax and Johnson & Johnson: Lower vaccine efficacy in South Africa compared to settings without the variant (press release data only). Moderate-severe disease were assessed. Serologic neutralization results pending.
- Oxford/AstraZeneca: Minimal vaccine efficacy against mild-moderate COVID-19 disease, with wide confidence intervals (press release data only), impact on severe disease undetermined. Serologic neutralization substantially reduced compared with original strains, based on small number of samples analyzed.

WHO Map of 14 Nations with P.1 Variant
Feb 9 WHO Weekly Epi Update



WHO Map of 32 countries with P.1 Variant
March 9 WHO Weekly Epi Update



20J/501Y.V3 B.1.1.28.1, alias P.1

- Transmissibility: increased -- more transmissible than previous circulating variants
- Severity: Under investigation, limited impact
- Vaccines – under investigation

Based on preliminary investigations in Manaus, where this variant was initially identified, P.1 has shown to have increased transmissibility compared to previously circulating variants. It can evade 25% to 61% protective immunity provided by the previous infection, thereby making people susceptible to reinfection[6]. Additionally, it is 1.1–1.8 times more likely to result in mortality. Researchers have cautioned that these are preliminary findings and the results are not generalizable to other settings. More studies and genome sequencing data are required to assess the transmissibility and severity of variant P.1. It is also important to conduct these studies outside of Manaus as there has been a sharp increase in hospitalizations during the second wave which has resulted in collapsing of health systems in Manaus (figure 9). Therefore, it is difficult to determine the cause of high mortality which could be either due to variant P.1 or collapsed health systems or both.

Key Point: We Will Need Multivalent Vaccines for Multivariant Viruses

- Need new vaccines against the variant 501Y.V2 (B.351) that is dominant in several nations in southern Africa.
- Will likely need new vaccines against the variant P1. (B.128) dominant in Manaus, northern Brazil.
- Why? Same 4 key mutations as in 501Y.V2 (N501Y, D614G, E484K, K417N) that increase transmissibility and impair antibody response.
- Other variants are being recognized.

Global demand for COVID-19 vaccines

- range from ~10-14 billion doses in 2021
- Herd immunity: working estimate is 70%, or about 5.5 billion people worldwide
- 11 billion doses of a two-dose regimen (subject to change if new variants are more transmissible).
- Manufacturers have announced a supply target of up to 14 billion doses – this would triple previous annual vaccine output
- Disparity will persist in the majority of 2021 in any scenario:
  - Favourable scenario: most demand could be met by the end of 2021
  - less favourable: disparity could persist for much longer
- significant geographical demand and supply imbalances.

TRIPS WAIVER

- There is a need for expanded manufacturing capacity while building on existing mechanisms to sustain and scale current investments that the Vaccine Alliance has achieved thus far
- Proposal under consideration at WTO that would allow countries not to grant or enforce intellectual property protections established in the TRIPS Agreement for vaccines, treatments and other medical products needed to control COVID-19 until the pandemic is over
- This is not some radical overhaul or erosion of IP rights and laws – it is a swifter way to exercise the provisions that already exist in international law which enable countries to waive IP protections in times of public health emergency
- Advantage of the waiver is that it enables countries to coordinate what they would otherwise have to on a country-by-country, case-by-case, product-by-product basis and removes bureaucratic obstacles→ we must prioritize lives over paperwork
- It is time-limited→ only until we reach herd immunity (IP rights can be enforced after)
- It does not interfere with IP protections afforded under countries' national laws

CTAP

- Some pharmaceutical companies have taken positive steps
  - Agreeing not to enforce patents (Moderna)
  - Voluntary licensing agreements with generic manufactures (AZ, Novavax)
  - Making vaccines available at cost until pandemic is over (AZ)
- But these steps don't get us far enough
- No pharmaceutical company has signed on to C-TAP, the WHO mechanism for IP sharing, technology & data transfer that would allow us to scale up global manufacturing
- Pharmaceutical companies' inability to manufacture the vaccine at the scale needed cannot stand as the barrier to ending the pandemic.
- Nearly one-third of vaccines have fewer than 4 suppliers

Equitable ‘accessibility’

- means vaccines must be
- economically accessible (affordable)
- geographically accessible (not only available in cities but in rural areas as well)
- accessible to vulnerable groups the disabled/differently abled, the aged, ethnic minorities, refugees and guest workers
- Government regulation prior to vax rollout

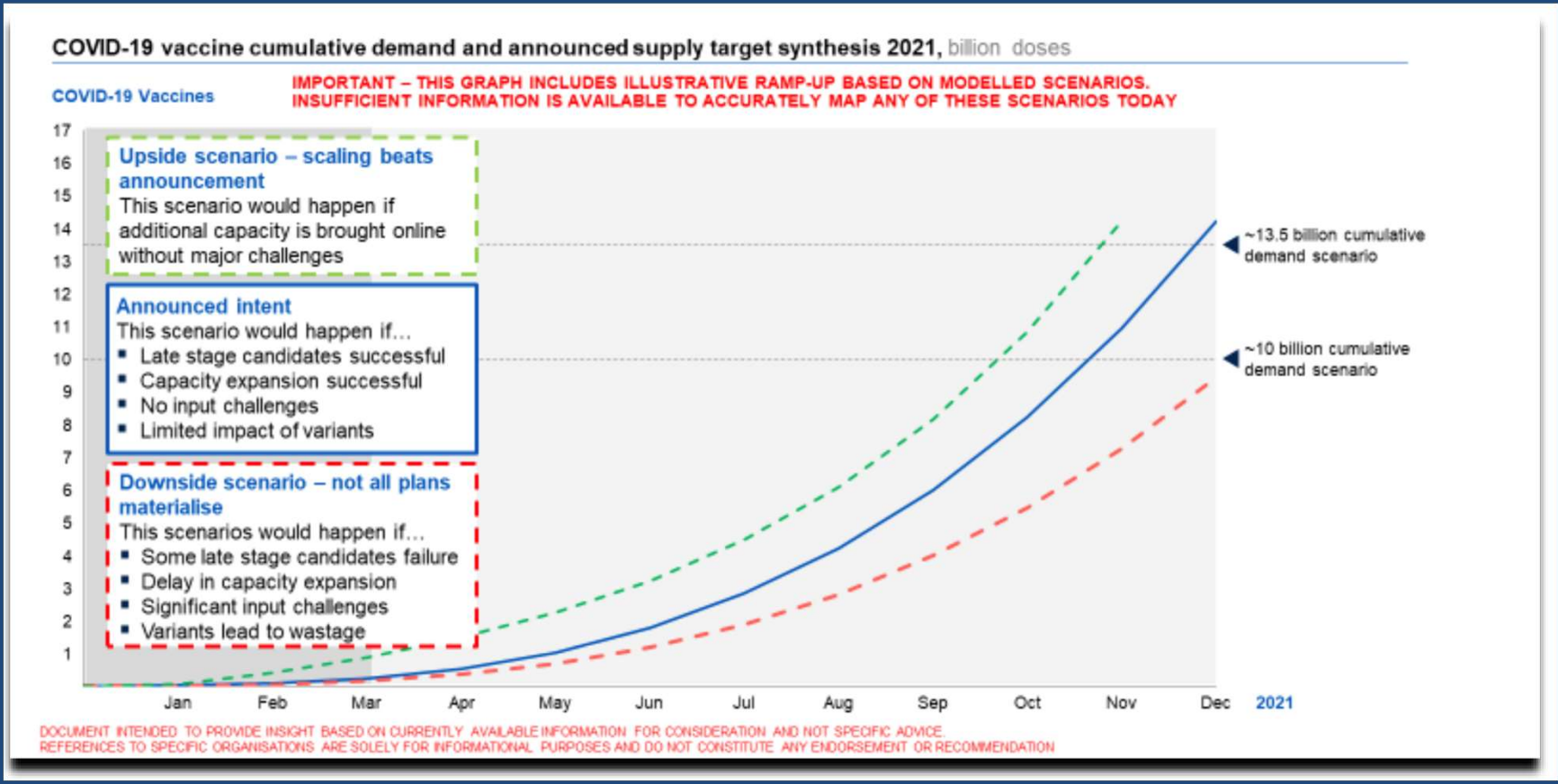
Vaccine producers by continent

with stage 3 products and later

Five questions remain regarding COVID-19 vaccine demand:

1. How much additional volumes will be procured for 2021 and beyond?
2. What is the need and frequency for boosters? How does this affect 2021 demand?
3. How will inefficient supply chains affect demand (e.g. expiration of products, hoarding behaviours due to erratic market developments)?
4. How will donations and exchanges (e.g. via COVAX) influence order patterns and volumes?
5. What will demand in 2022 and beyond look like and what are the supply implications?

COVID-19 Vaccine Cumulative Supply and Demand Synthesis 2021



Potential Supply Chain Challenges Along Vaccine Manufacturing Value Chain

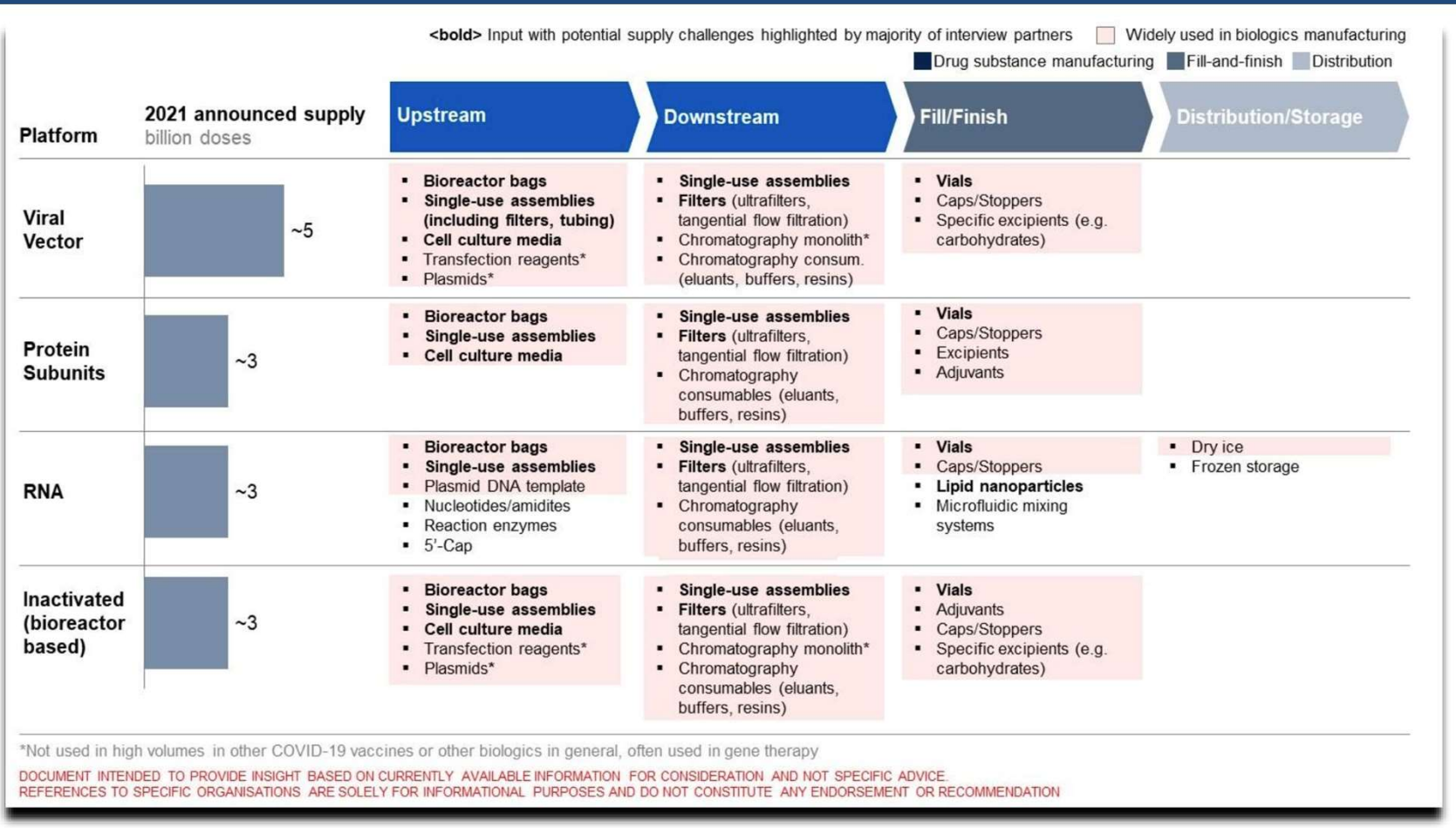
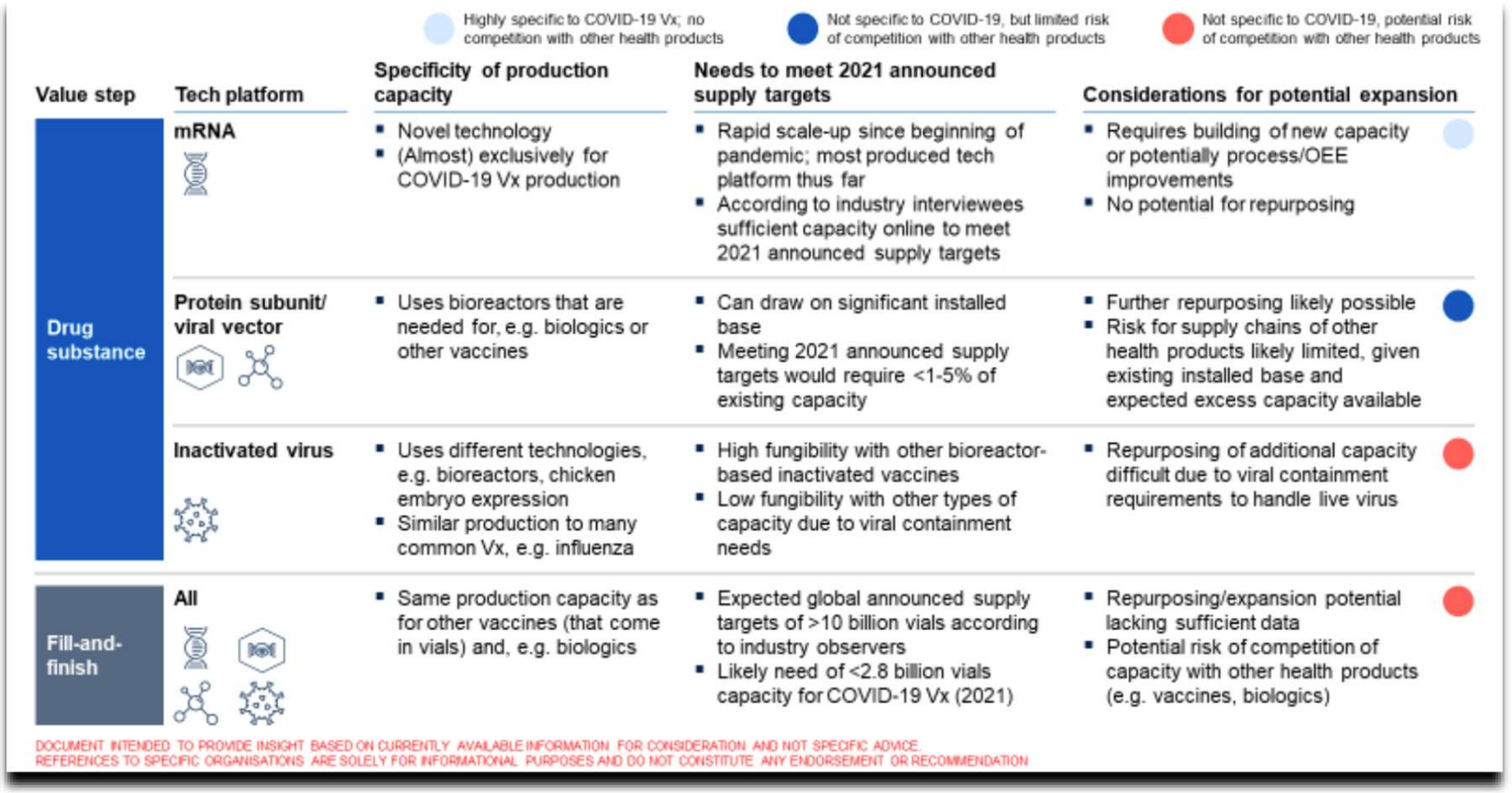


Exhibit 8 – Overview of Manufacturing Capacity by Platform



Value step	Tech platform	Specificity of production capacity	Needs to meet 2021 announced supply targets	Considerations for potential expansion
Drug substance	**mRNA**	▪ Novel technology ▪ (Almost) exclusively for COVID-19 Vx production	▪ Rapid scale-up since beginning of pandemic; most produced tech platform thus far ▪ According to industry interviewees sufficient capacity online to meet 2021 announced supply targets	▪ Requires building of new capacity or potentially process/OEE improvements ▪ No potential for repurposing
	Protein subunit/ viral vector	▪ Uses bioreactors that are needed for, e.g. biologics or other vaccines	▪ Can draw on significant installed base ▪ Meeting 2021 announced supply targets would require <1-5% of existing capacity	▪ Further repurposing likely possible ▪ Risk for supply chains of other health products likely limited, given existing installed base and expected excess capacity available
	Inactivated virus	▪ Uses different technologies, e.g. bioreactors, chicken embryo expression ▪ Similar production to many common Vx, e.g. influenza	▪ High fungibility with other bioreactor-based inactivated vaccines ▪ Low fungibility with other types of capacity due to viral containment needs	▪ Repurposing of additional capacity difficult due to viral containment requirements to handle live virus
Fill-and-finish	**All**	▪ Same production capacity as for other vaccines (that come in vials) and, e.g. biologics	▪ Expected global announced supply targets of >10 billion vials according to industry observers ▪ Likely need of <2.8 billion vials capacity for COVID-19 Vx (2021)	▪ Repurposing/expansion potential lacking sufficient data ▪ Potential risk of competition of capacity with other health products (e.g. vaccines, biologics)

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