

December 6, 2020

Global COVID-19 Vaccine Syringe Supply Assessment

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Project objectives

With an impending COVID-19 vaccine in late 2020/2021, Gavi has initiated coordinated supply planning activities for the new vaccine and associate products, including syringes, vials, and cold chain equipment. There is a specific and urgent need to conduct a deeper assessment of the syringe market to ensure production volumes can be secured with no delay for **the 92 low- and lower-middle income countries (LMICs)*** that will be rolling out vaccines **under the COVAX Advance Market Commitment (AMC)**.

This work will aid UNICEF, Gavi, and the COVAX facility in its coordinated supply planning efforts by executing a market assessment of global syringe capacity.

The objectives of this work are:

1. Assess the auto-disable (AD) and reuse prevention (RUP) syringe and safety box market, with a focus on the World Health Organization (WHO) prequalified suppliers.
2. Establish different scenarios for ensuring syringe supply, with considerations for decision points in the value chain.
3. Evaluate and model risks in supply and demand matching and provide recommendations for mitigating actions.
4. Continue to monitor the syringe market for fluctuations.

³ *11 International Development Association-eligible countries are also included in the count of 92 countries covered by the COVAX AMC.

Products in scope given potential utility for COVID vaccination

	Uses/status	Scope priority
AD syringe with feature activation at the <u>start</u> of the injection stroke (0.5 mL)	Currently exclusively supplied by UNICEF for vaccines. Expected to be standard for LMIC delivery of COVID vaccines. Also may be procured by some upper middle- and high-income governments for COVID vaccines.	Top priority (expected dose volume for COVID vaccines)
AD syringe with feature activation at the <u>end</u> or <u>middle</u> of the injection stroke (0.5mL)	Can be WHO prequalified but are not supplied by UNICEF. Currently used in some domestic markets for vaccine delivery. Also may be procured by some upper middle- and high-income governments for COVID vaccines.	Secondary priority (expected dose volume for COVID vaccines)
RUP syringe (5 mL & 10 mL)	Currently supplied by UNICEF and used for vaccine reconstitution. A subset of COVID vaccines need reconstitution or mixing before use. (One syringe per multidose vial.)	Lower priority (expected dose volume for COVID vaccine reconstitution)
Safety boxes (5 L)	All used disposable syringes should be disposed of in a safety box. The majority of UNICEF suppliers bundle syringe and safety boxes into one shipment. Consolidation of bundled supply can happen at UNICEF warehouses. Estimated ratio is 100 syringes per safety box.	Lower priority

Notes: In scope syringes were selected in consultation with the Bill & Melinda Gates Foundation with the expectation that injectable vaccines supplied to COVAX will have 0.5 mL dose volume and be in multidose vials. Some COVID vaccines have different dose volumes. For definition of terms, please see the Appendix.

Products in scope for COVID vaccination

AD syringe with feature activated at **start** of the injection stroke (0.5 mL)*

Examples:

- BD Soloshot
- Sanavita Helmject
- ADMD Medeco



AD syringe with feature activated at **middle or end** of the injection stroke (0.5 mL)*

Examples:

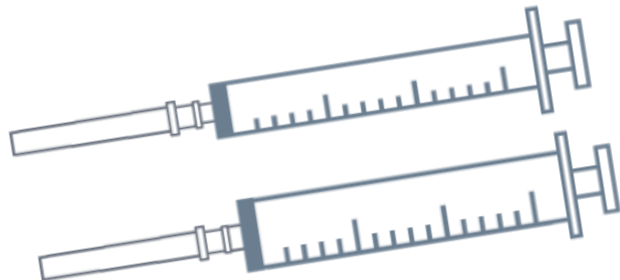
- Retractable Technologies Vanishpoint
- Oneject K1



RUP syringe (5 mL and 10 mL)

Examples:

- BD Emerald Pro
- HMD Kojak Selinge



Safety box (5 L)

Examples:

- Pa-Hu Oy
- Tim Safe
- Kojak SB



*Alternate-dose AD syringes (like 0.3mL syringes for Pfizer's vaccine) would be manufactured on the same lines and production capacity could be substituted.

Key findings

RUP syringes and sharp boxes have adequate supply

- Supply far outweighs demand for all scenarios and years
- Model assumes 20% of vaccines will require mixing and 100 syringes per safety box

AD syringe capacity is adequate in all scenarios if both **start** and **end** activation are used

- If only start activation syringes are used, existing syringe stockpile (520 million units) can be used to help meet the demand in 2021
- In 2022 and beyond, additional investment in new manufacturing lines is needed if only start activation syringes are used

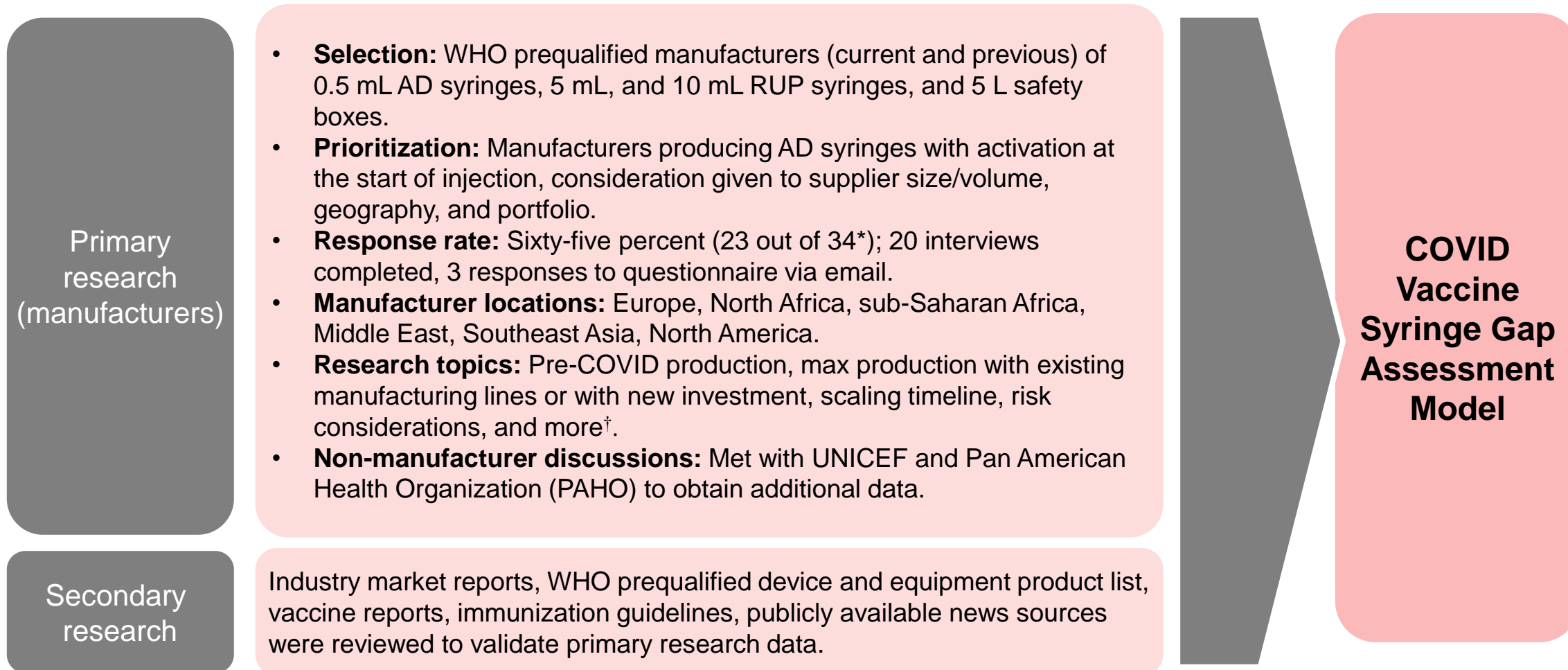
Long shipping times, warehousing capacity and market uncertainty present key challenges

- Syringes primarily ship by sea with lengthy shipping times (up to 10 weeks)
- Existing syringe stockpile will likely need to be used in Q1 2020 given long shipping times
- Many manufacturers can only store syringes for one month, but can rent additional space with advance notice and budget
- Manufacturers desire to have more visibility in the market highlighting the need for targeted communication and outreach

Key limitations

- Syringe demand scenarios are based on current modeling of the number of vaccine doses produced, and analysis will be updated as new vaccine dose estimates become available
- Uncertainty about demand for AD syringes for COVID vaccination in UMICs and HICs as precise estimates are unknown

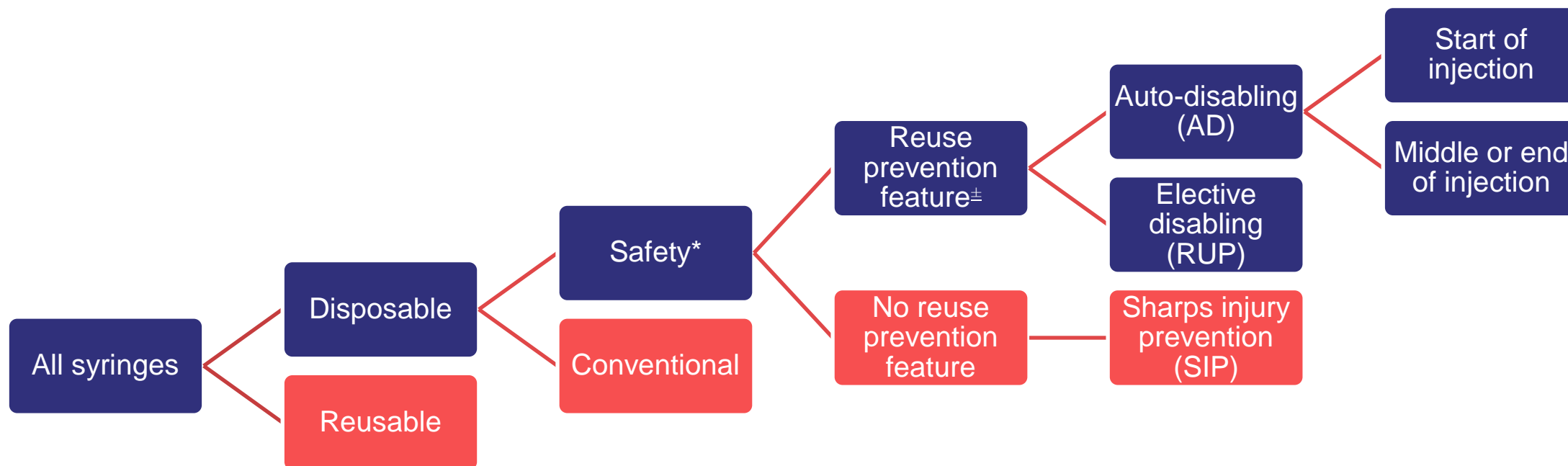
Research methods to inform inputs into the gap assessment model



* Manufacturers currently in business and producing syringes in scope (PATH analysis). Based on website review, non-respondents appear to be primarily domestic suppliers.

† See appendix for additional details on research topics and supply scenarios.

Syringe market segmentation reveals various types of safety devices with reuse and injury prevention mechanisms



■ Focus of current assessment

*Syringe with sharps injury prevention, reuse prevention, and/or auto-disable mechanism.

± Syringes with reuse prevention features can also include a variety of sharps injury protection features depending on the design.

AD syringes are a small share of the global market, used almost exclusively in low- and middle-income* countries for immunizations

Safety syringe products

- Safety syringes account for the largest share of syringes in the global market and are expected to remain dominant due to cost-effectiveness, ease-of-use, and protection offered to patients and health care workers.
- Increased demand and competition has reduced prices to the point where no significant price difference exists between conventional disposable syringes and many safety disposable syringes.

Syringe usage

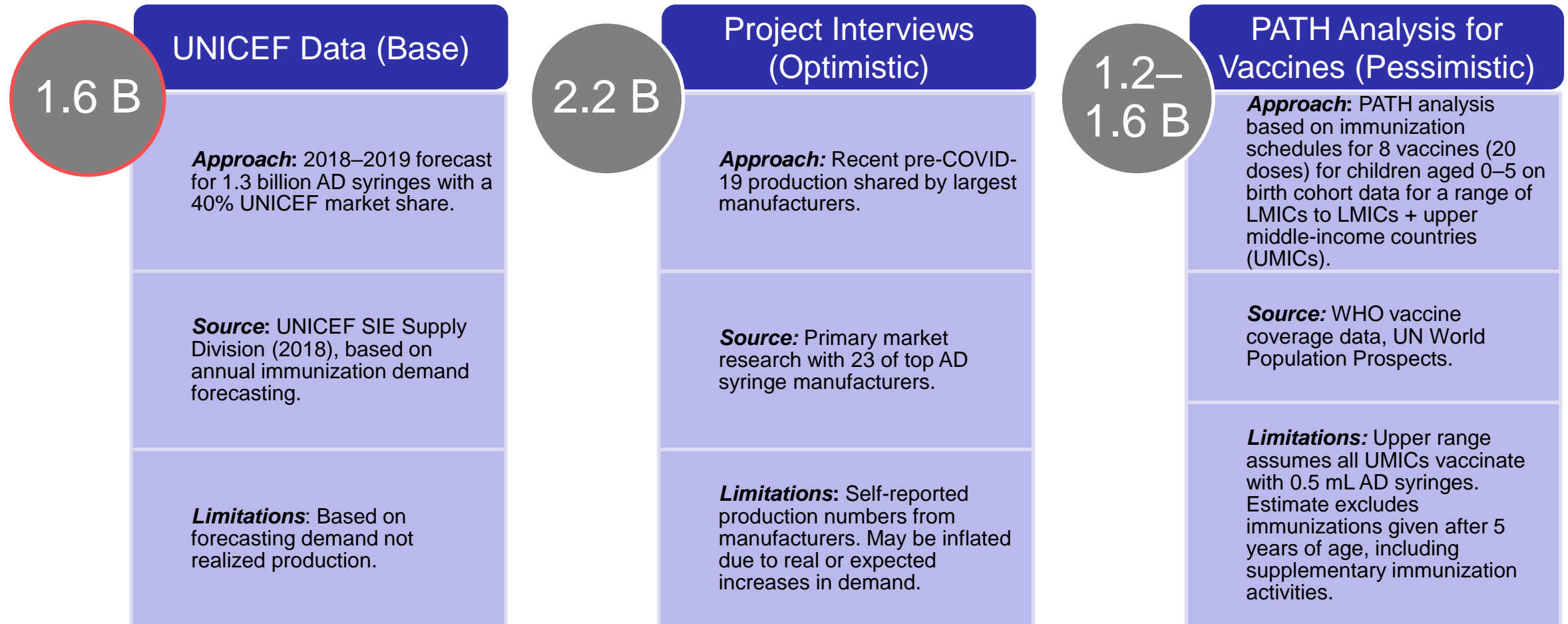
- Approximately 10 percent of global disposable syringes are used for immunizations, with the remaining used for therapeutic injections and blood collection and transfusion.
- Only AD syringes are WHO prequalified for immunization injections and are used almost exclusively for this purpose due to the limitation of having a fixed-dose volume.

Regional trends

- While North America has consistently been the largest buyer in the safety syringe market, most high-income countries almost exclusively rely on prefilled, SIP, and retractable needle syringes rather than AD for immunization.
- The Asia Pacific region has seen the highest growth in the AD market due to mass immunization programs and growing health care expenditure and per capita income.
- Increased presence of local manufacturers, specifically in Asia and North Africa/Middle East, has stimulated local acceptance, reduced delivery and production costs, and helped to build markets for AD syringes.

*This includes low-, lower middle-, and upper middle-income.

Three approaches used to estimate pre-COVID-19 annual market size for AD syringes ranging from 1.2–2.2 billion syringes



AD syringe market has several opportunities, but potential challenges exist due to inefficiencies from long lead times and geographic spread

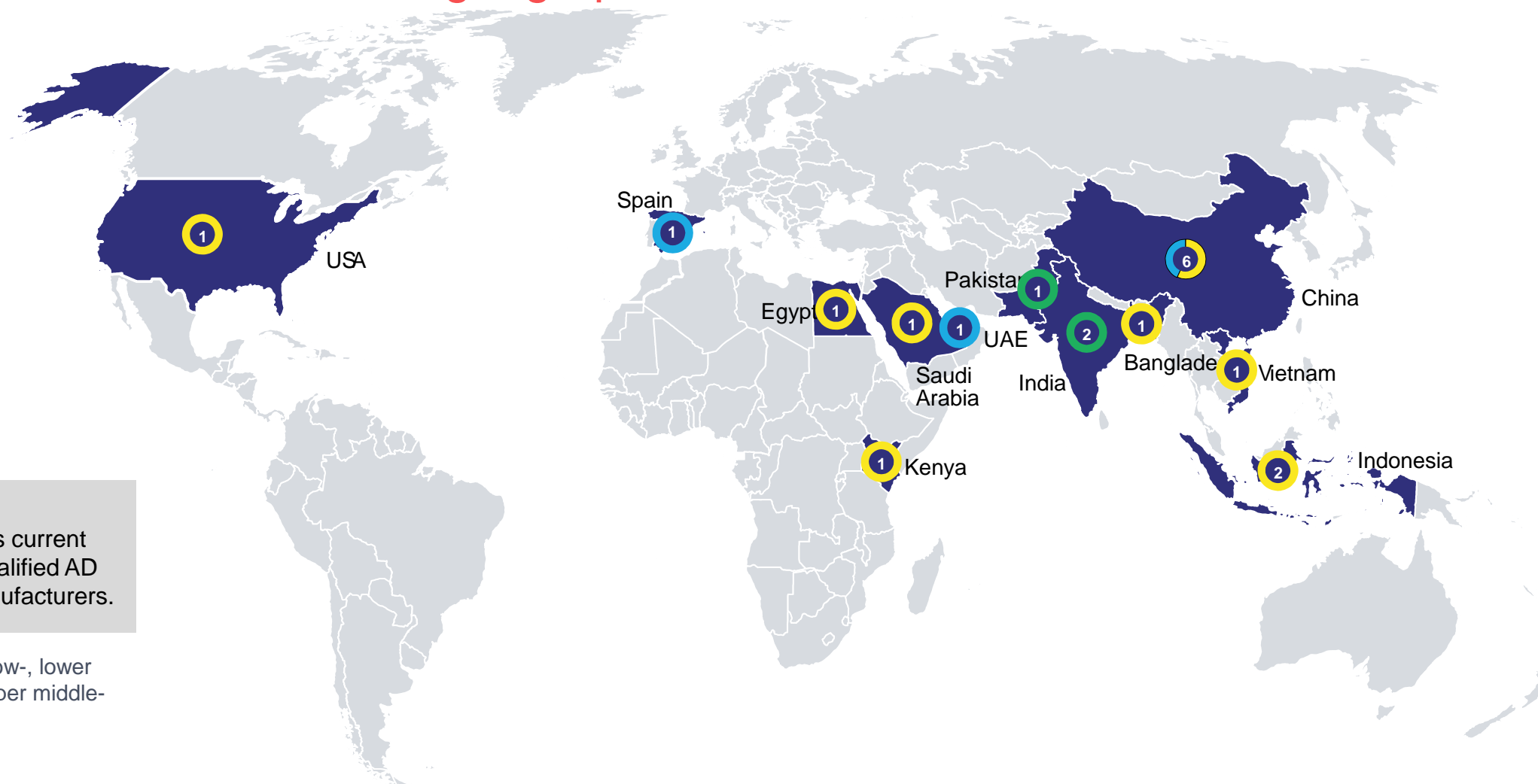
Opportunities

- Rising concern over accidental or intentional reuse.
- More stringent government regulation around patient safety and security.
- Good supply base for quality assured injection devices.
- Long shelf life for product (up to 5 years).
- Engaged partners and established partner forums.
- Expanding immunization programs.
- Price of AD syringes comparable with conventional disposable syringes due in large part to consolidating purchasing power from UNICEF procurement (~40% of immunization market).
- Increasing geographic spread and local manufacturing capacity.

Challenges

- Long lead times required for sea transport (1–4 months), air travel possible but expensive due to product bulkiness and order sizes.
- Significant storage capacity required due to bulkiness of product (~43cm³ per unit).
- Geographically spread supply base can create inefficiencies in supply chain.
- Multiple vaccines and immunization program needs influence demand.
- Effective waste management is still challenging.

AD 0.5 mL syringes are manufactured and warehoused predominantly in low- and middle-income* geographies



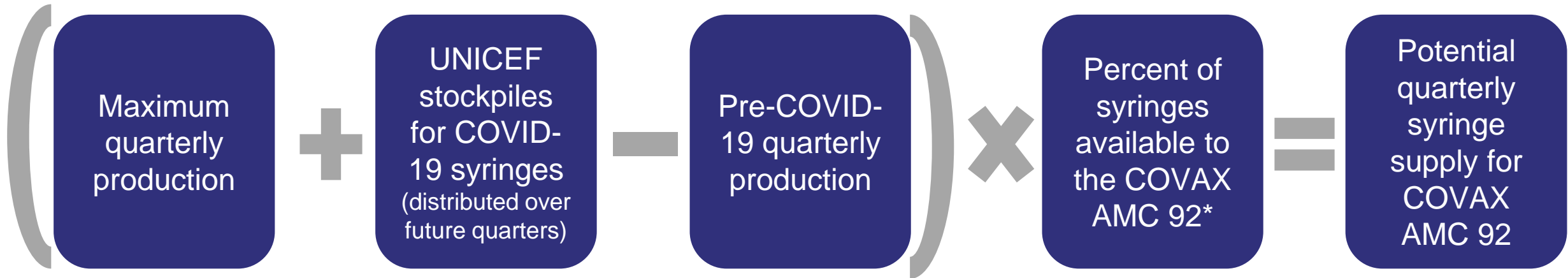
Notes:

- Data reflects current WHO prequalified AD syringe manufacturers.

*This includes low-, lower middle-, and upper middle-income.

AD syringe manufacturing locations Start of injection End of injection Start and end of injection

Calculating the COVID-19 vaccine syringe potential supply

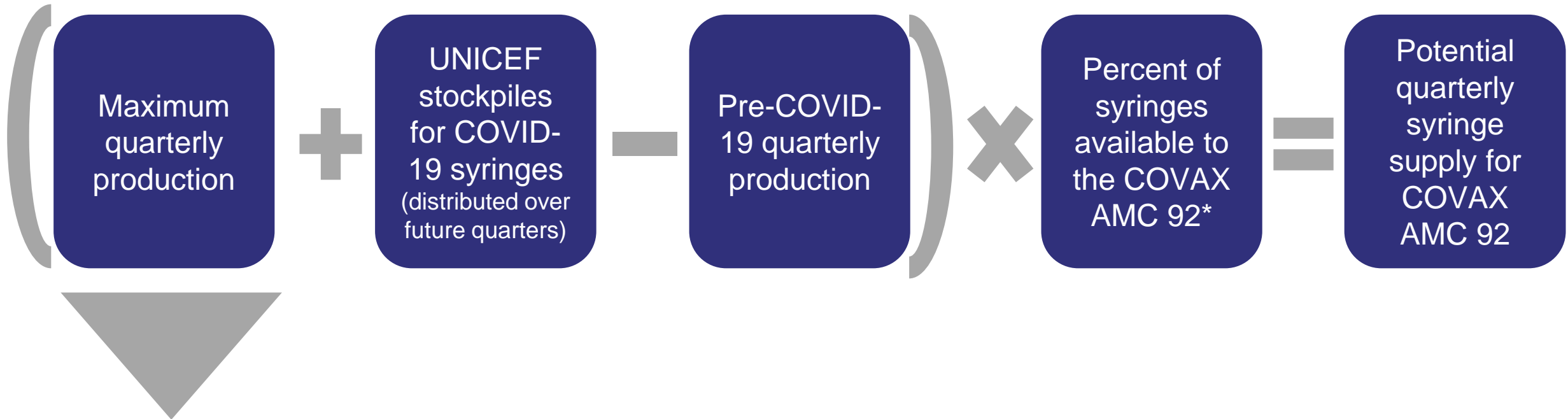


Model timeframe is three years.

Analysis was calculated separately for 0.5 mL AD syringes, 5 mL RUP syringes, and 10 mL RUP syringes.

*Estimation of the percentage of available syringes for COVID-19 vaccination that will not be procured for use in UMICs and high-income countries (HICs).

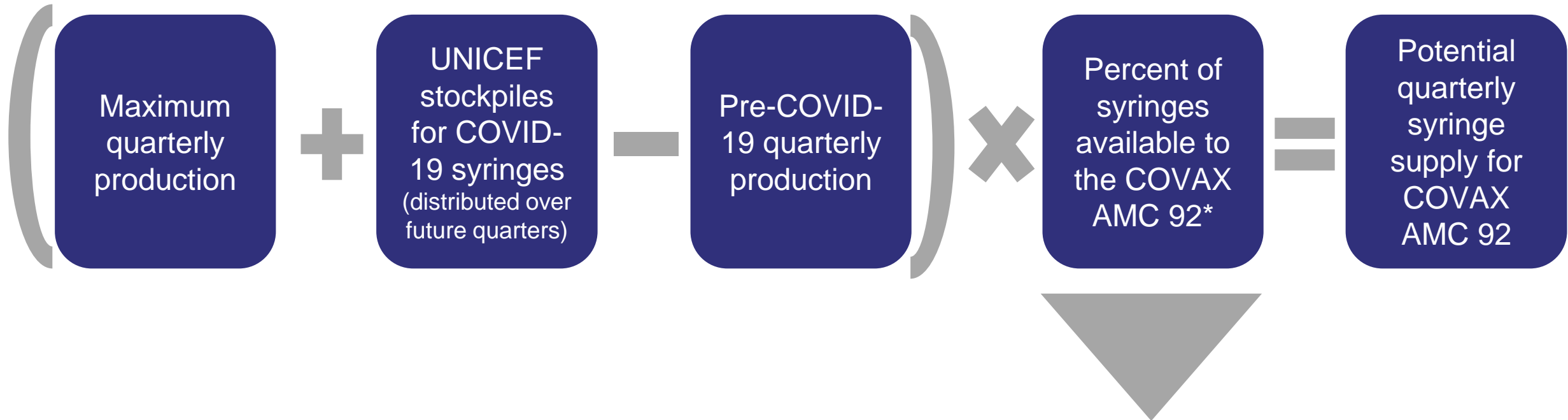
Calculating the COVID-19 vaccine syringe potential supply



Two different supply scenarios were evaluated:

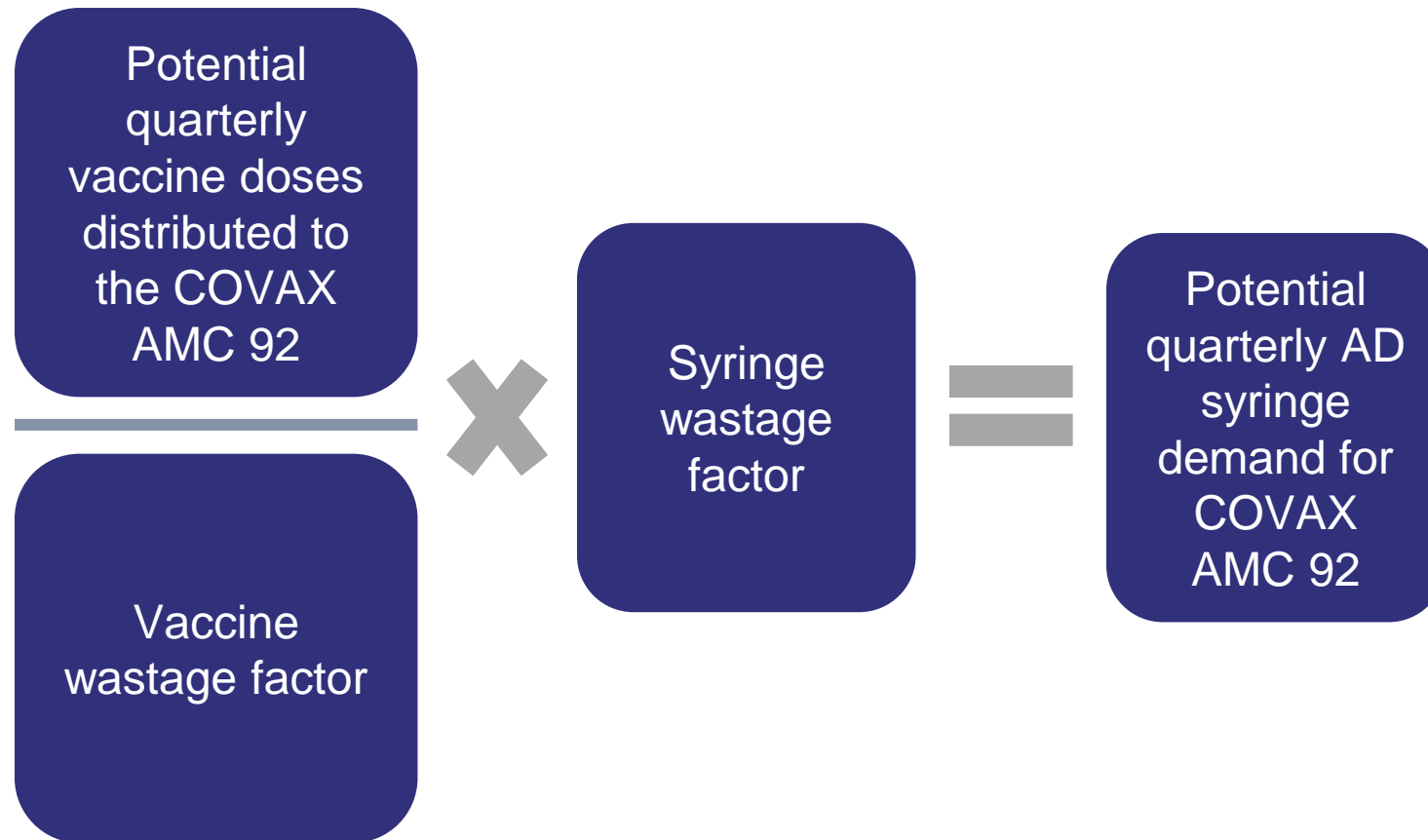
- 1) Maximum production using existing lines.
- 2) Maximum production using existing lines plus adding additional capacity with new investment.

Calculating the COVID-19 vaccine syringe potential supply



Of the additional syringe production capacity that could be available for the COVID-19 vaccination, a portion is likely to be used by UMICs and HICs. Many UMICs and a few HICs (e.g. PAHO) routinely use AD syringes for immunization.

Comparing the COVID-19 vaccine syringe supply with the demand to estimate the potential gap



Potential quarterly syringe supply was **compared** to the estimated number of vaccine doses to estimate the potential gap.

Estimated number of vaccine doses are used as a proxy for syringe demand (actual desire to get vaccinated is currently unknown)

Syringe supply was shifted one quarter later than manufacturers stated due to the long typical shipping times (up to 10 weeks).

*Wastage factor = $100 / (100 - \text{wastage rate})$

Syringe demand (vaccine supply) scenarios

Vaccine supply forecasting was provided by Linksbridge from their review of COVAX vaccine deals and considering the probabilities of regulatory approval and manufacturing output (December 1st analysis).

Three vaccine supply scenarios were used, from 10,000 simulations in their model:

- 1) Low – 20th percentile
- 2) Average – mean (“realistic” scenario)
- 3) High – 80th percentile

Based on the relative target populations of AMC and self-financing COVAX countries, and assuming equitable distribution across all COVAX countries, **67% of the total vaccine doses** available to COVAX were assumed by PATH to be targeted to the 92 AMC countries.

As COVAX has not completed vaccine deals for 2022 and beyond, we assumed **peak-level vaccine supply in 2021 remains constant** in future years.

Key supply model assumptions and rationale that can be adjusted in the model

Variable	Default Input	Source/Rationale
Percent of COVID-19 AD syringes that go to COVAX AMC countries	70 percent	PATH analysis that assumed that all UMICs (excluding China) and PAHO HICs (excluding US/Canada) will procure AD syringes. (COVAX AMC population / [COVAX AMC + UMIC – China + PAHO HIC population.] Assumes COVID-19 vaccine distribution is based on population.)
COVID-19 syringe stockpile data	520 million AD syringes No RUP syringes	Publicly available data on UNICEF stockpile procurement (country-level stockpile data not included in model and assumed to be low).
Distribution of stockpile syringes	Targeted to meet supply gaps.	Timeline on which quarters the stockpile will be distributed has not been provided to date. Stockpile assumed to be used to meet anticipated supply gaps.
Number of syringes with and without investment	Varies by quarter	Primary market research where manufacturers were asked what their pre-COVID-19 quarterly production was and their maximum quarterly production on existing manufacturing lines and with investment.
Number of safety boxes needed	1 box per 100 syringes	Based on WHO measles vaccine campaign planning guide.
Activation stage of AD mechanism	All syringes included in supply, regardless of activation stage	AD syringe supply can be toggled to include only syringes with activation at start of injection, only syringes with activation at end of injection, or all syringes.
UNICEF long-term agreement (LTA) status	All products included in supply, regardless of LTA status	Syringe supply can be toggled to include only products for which UNICEF currently has an LTA in place.

Key demand model assumptions and rationale that can be adjusted in the model

Variable	Default Input	Source/Rationale
Number of quarterly vaccine doses	Scenario based	Provided by Linksbridge (model results December 1, 2020).
Vaccine wastage rate	10 percent	Based on WHO measles vaccination campaign planning guide (10-dose vials, must be discarded after one vaccination session). COVID-19 vaccine wastage may differ.
Syringe wastage rate	10 percent	Based on measles campaign planning guide (default input for AD, 5 mL RUP, and 10 mL RUP).
Percent of vaccines requiring mixing	20 percent	Based on COVAX communication that a small proportion of vaccines will require reconstitution or mixing of separate adjuvant. The model allows for varying this proportion for vaccines in 5-dose, 10-dose, and 20-dose vials. Note that 5 mL RUP syringes are assumed to be used for 5-dose and 10-dose vials and 10 mL RUP syringes are assumed to be used for 20-dose vials.

Manufacturers can increase production with a purchase commitment; however, nearly all highlighted uncertainty in the market

Increasing production is possible

- Most can increase production by 100 percent or more with existing manufacturing lines.
- Some manufacturers stated that they are already ramping up production with existing manufacturing lines.
- Expanding production lines may require additional funding and confirmed orders prior to fund upgrade.

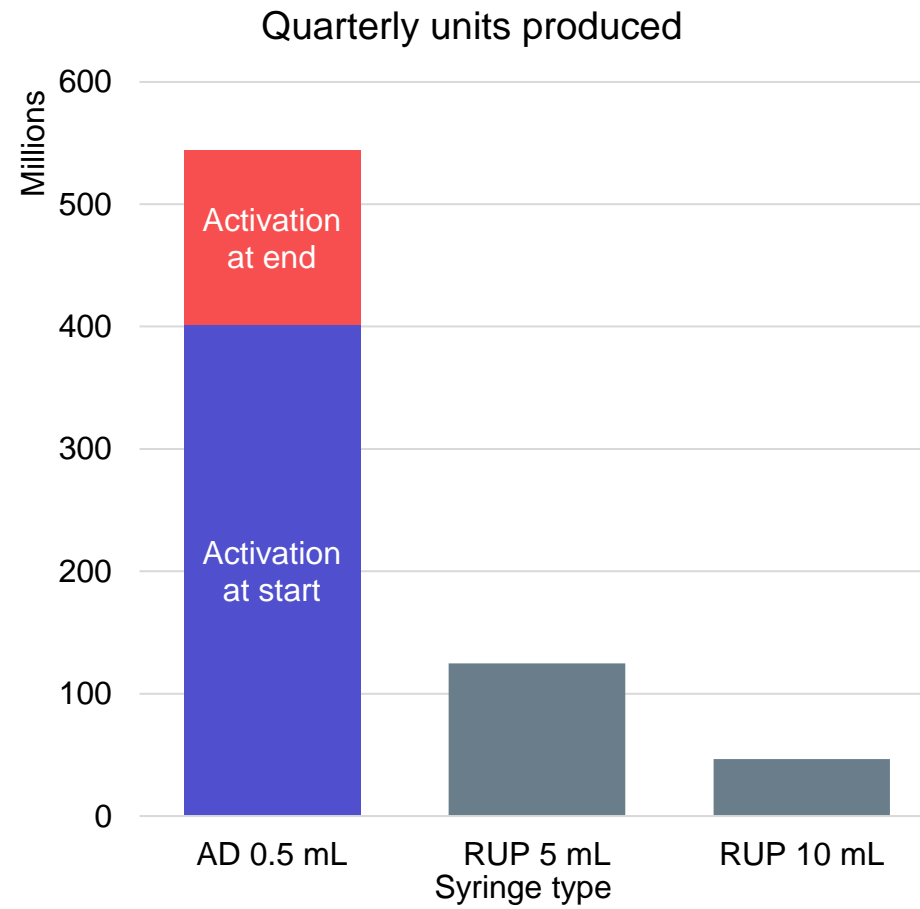
Lead times depend on desired capacity and required investment

- Reaching max surge production can be achieved within 1–6 months, varying by manufacturer.
- Reaching additional capacity (adding new lines) with increased investment can be achieved in 12–28 months.

Uncertainty in the market perceived as high risk

- No guarantee for sustained demand is a risk for increasing production capacity.
- Existing syringe stockpiles could result in fluctuations in demands.
- Manufacturers have received multiple requests for information related to COVID-19 syringe, but it is unclear how that translates to demand.
- Syringe types needed for COVID-19 vaccination have not been communicated to manufacturers.

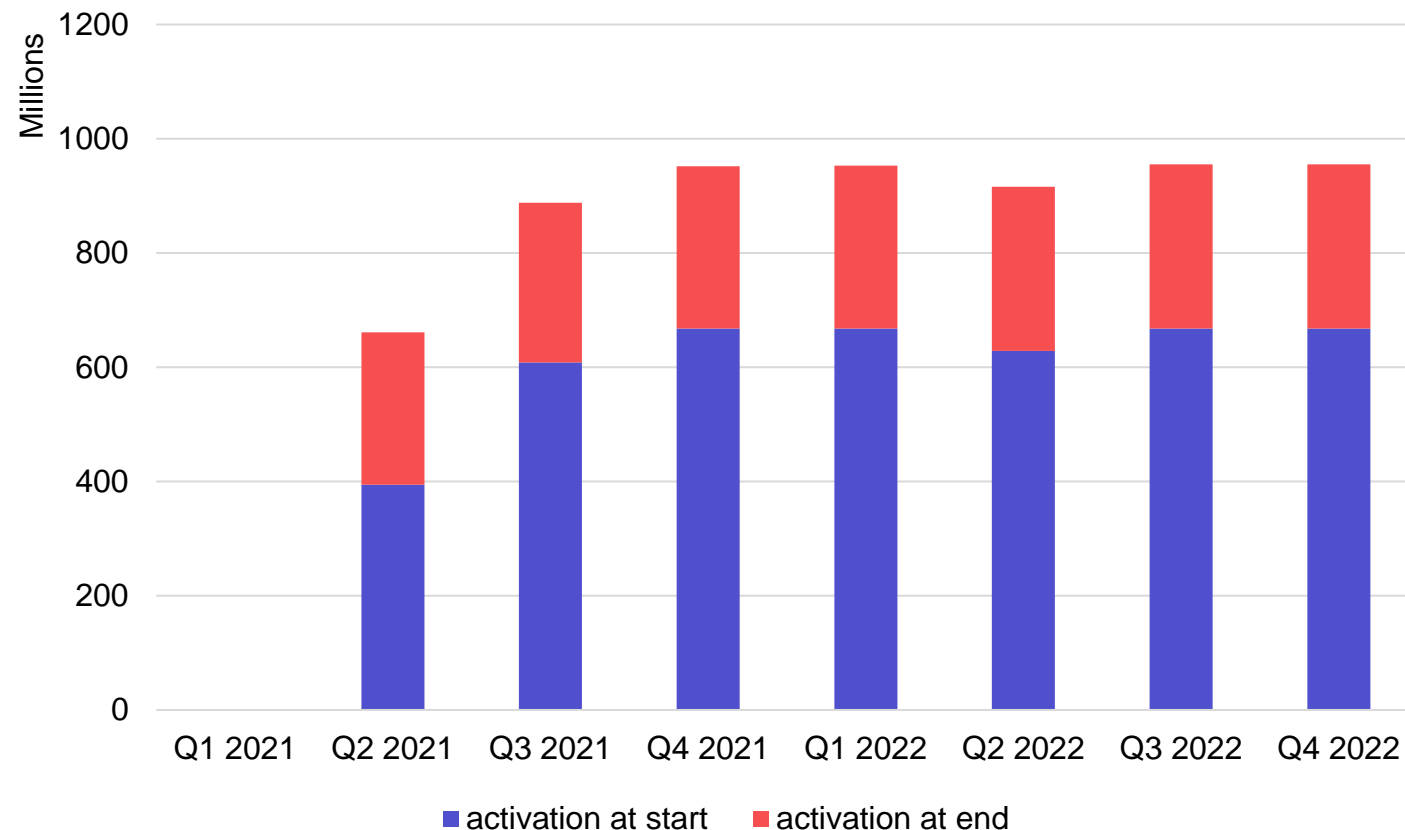
Primary market research findings suggest that pre-COVID-19 syringe production and market share are fragmented with no dominant player



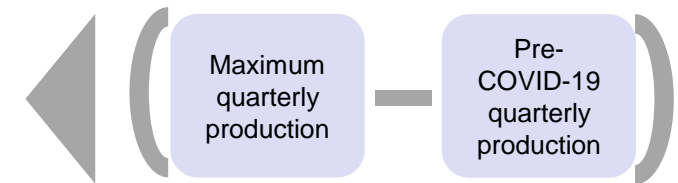
Pre-COVID-19 production also validated against vaccine demand data. See previous slides for more information.

Global AD syringe production can more than double with existing manufacturing lines

Global estimated number of AD syringe units available for COVID-19 vaccination



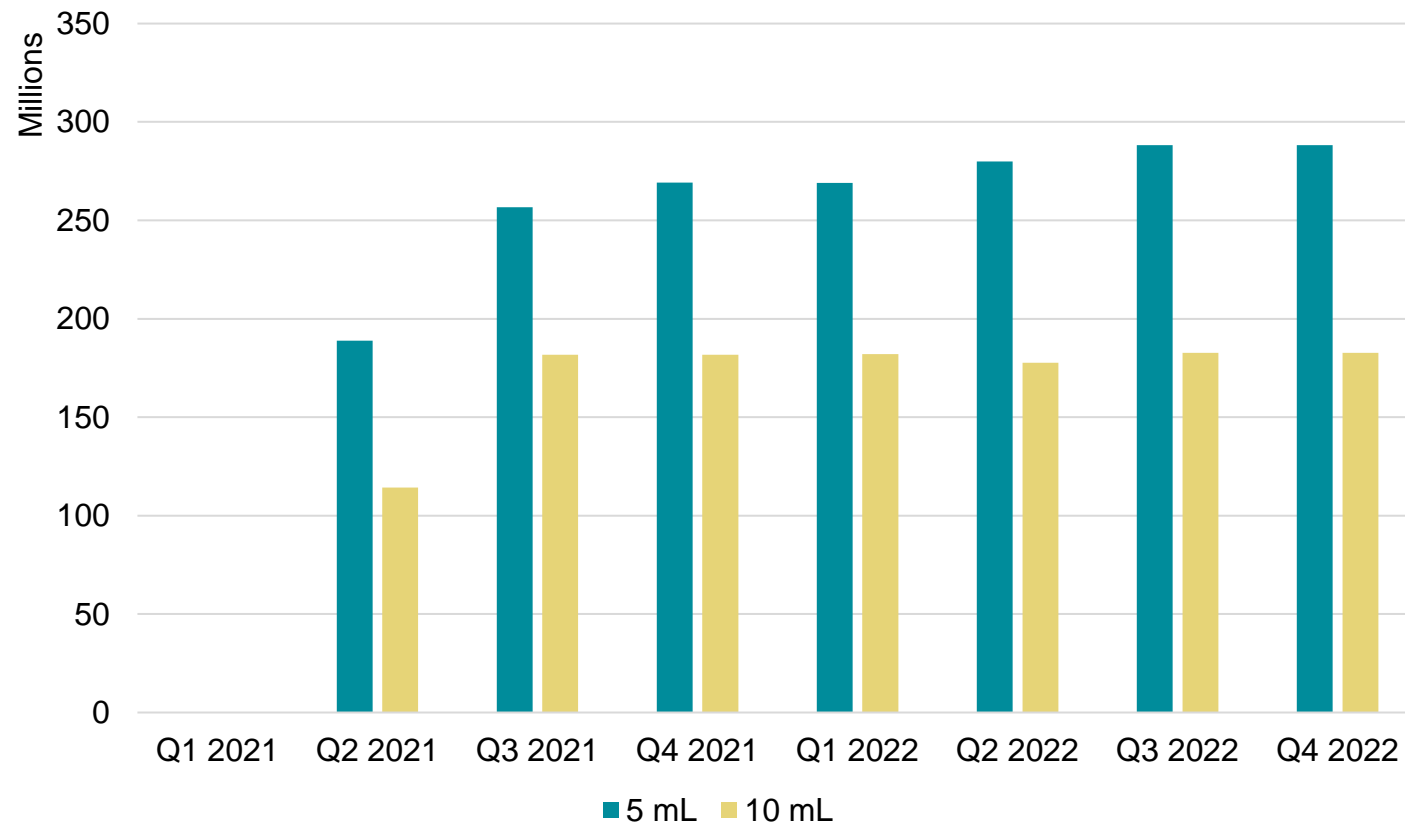
- Pre-COVID-19 syringe manufacturing volumes were estimated at 544M units quarterly by manufacturers
- Manufacturers estimate that they can produce 1.5B per quarter with existing manufacturing lines



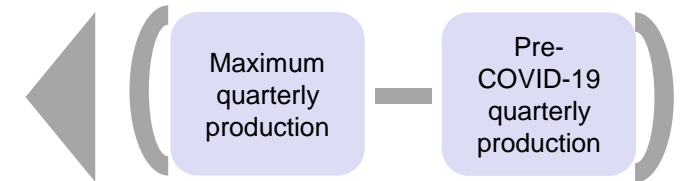
- Graph represents the number of units available for COVID-19 (Pre-COVID-19 volumes were subtracted)

Global RUP syringe production can more than triple with existing manufacturing lines

Global estimated number of RUP syringe units available for COVID-19 vaccination

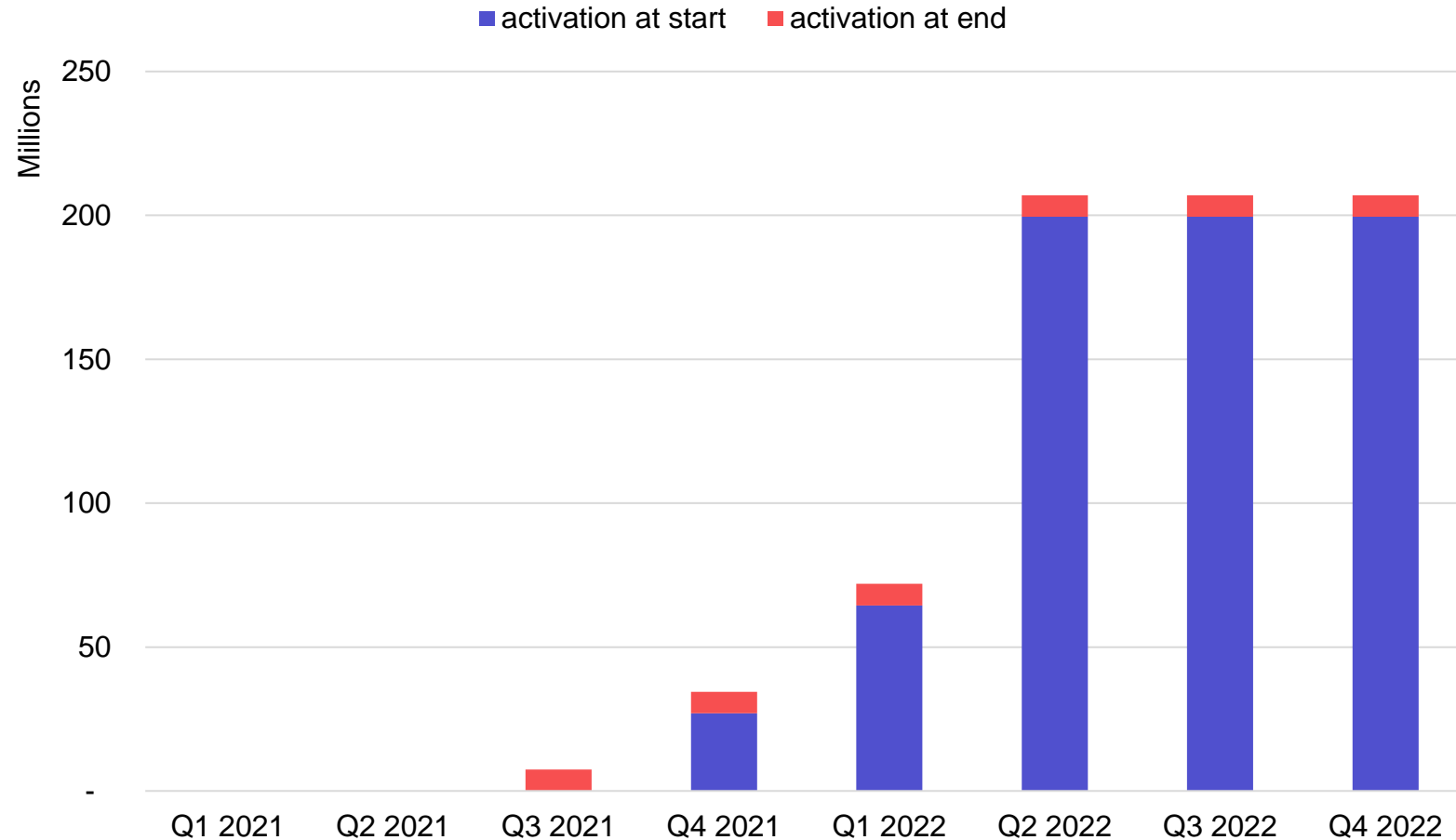


- Pre-COVID-19 syringe manufacturing volumes were estimated at 125M for 5 mL and 47M for 10 mL quarterly by manufacturers
- Manufacturers estimate that they can produce 413M for 5 mL and 229M for 10 mL per quarter with existing manufacturing lines



- Graph represents the number of units available for COVID-19 (Pre-COVID-19 volumes were subtracted)

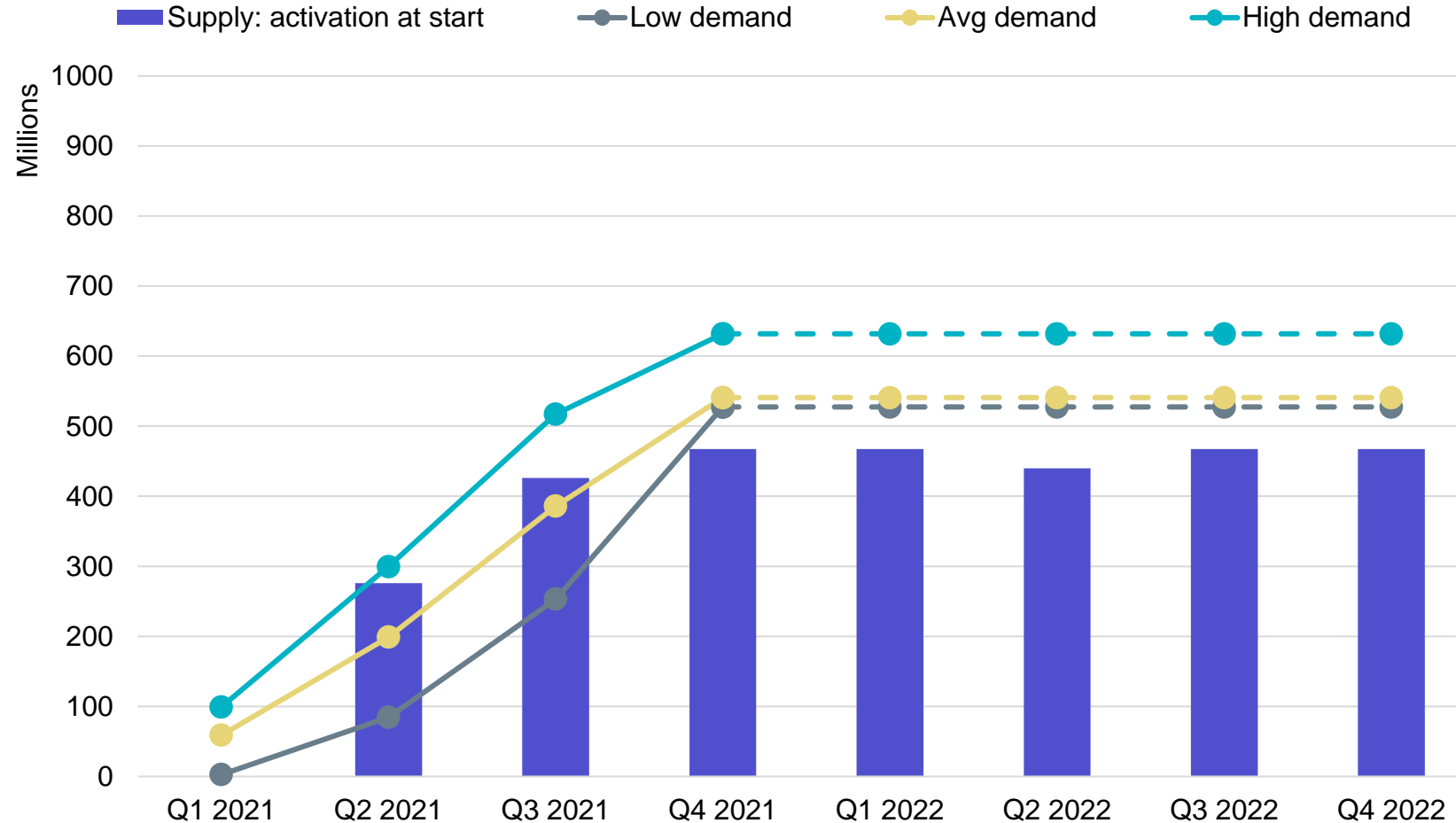
Select manufacturers were able to provide estimates on how new investment could spark additional production



Key findings:

- Most manufacturers indicated it would take 12+ months to produce syringes on new manufacturing lines.

AD syringe gap analysis suggests risk of inadequate supply if only start-activation AD syringes are desired



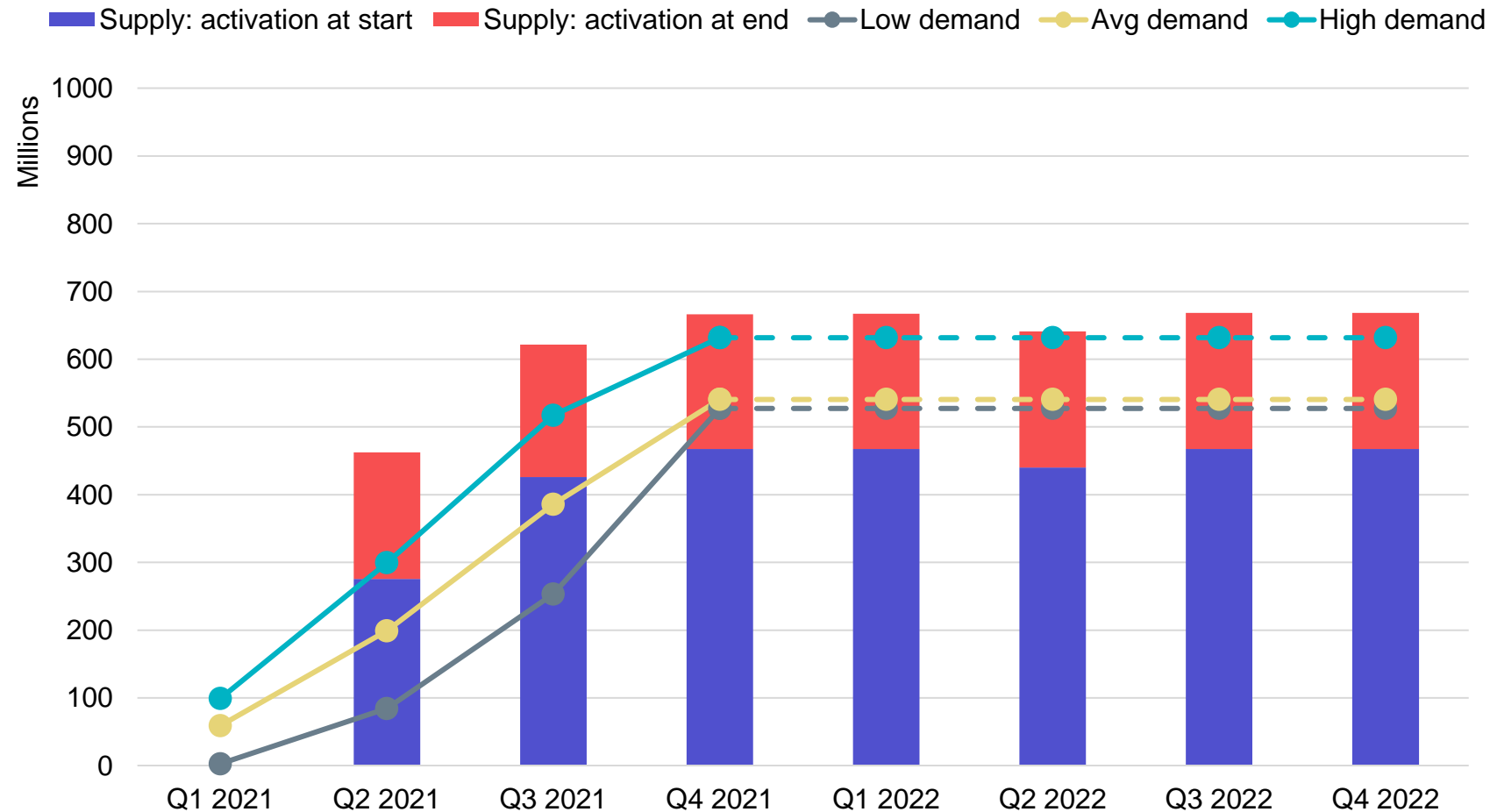
Key findings:

- Inadequate supply if only start activation syringes are used.
- Need for syringes in 2022 and beyond is highly uncertain and dependent on new deals made (model assumes the same value for Q4 2021 is maintained in future quarters).

*Supply data shown assumes 70 percent of COVID-19 syringe supply is available to the COVAX AMC countries.

**Demand forecasts as of Dec 1 2020.

Adequate supply seen in most scenarios if both start- and end-activation syringes are used



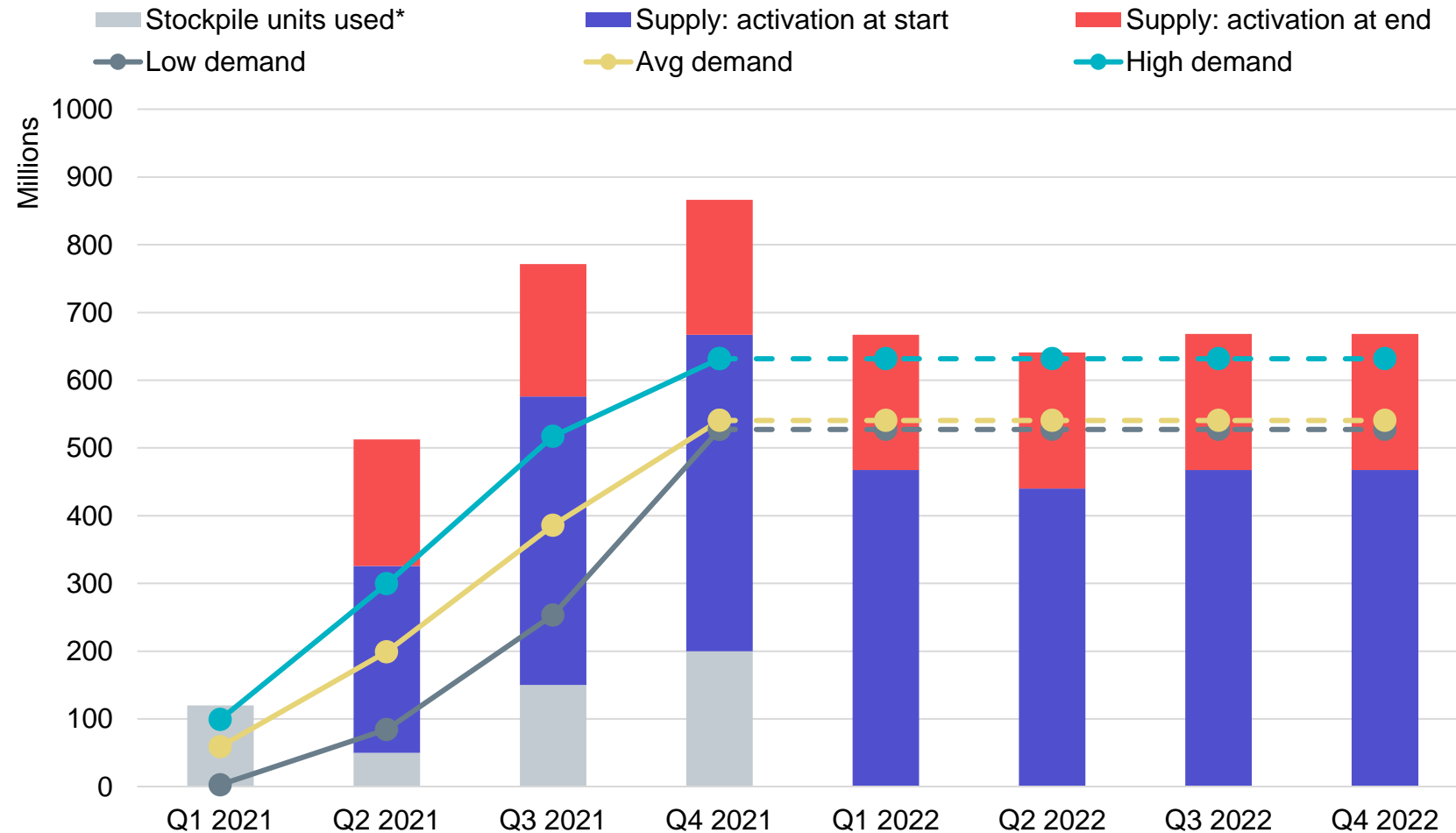
Key findings:

- Supply expected to meet demand for low, average and high forecasts if start and end of activation syringes are used.
- UNICEF policy currently is not to procure end of activation AD syringes for vaccine delivery.

*Supply data shown assumes 70 percent of COVID-19 syringe supply is available to the COVAX AMC countries.

**Demand forecasts as of Dec 1 2020.

Use of stockpile to address potential AD syringe supply gaps



Key findings:

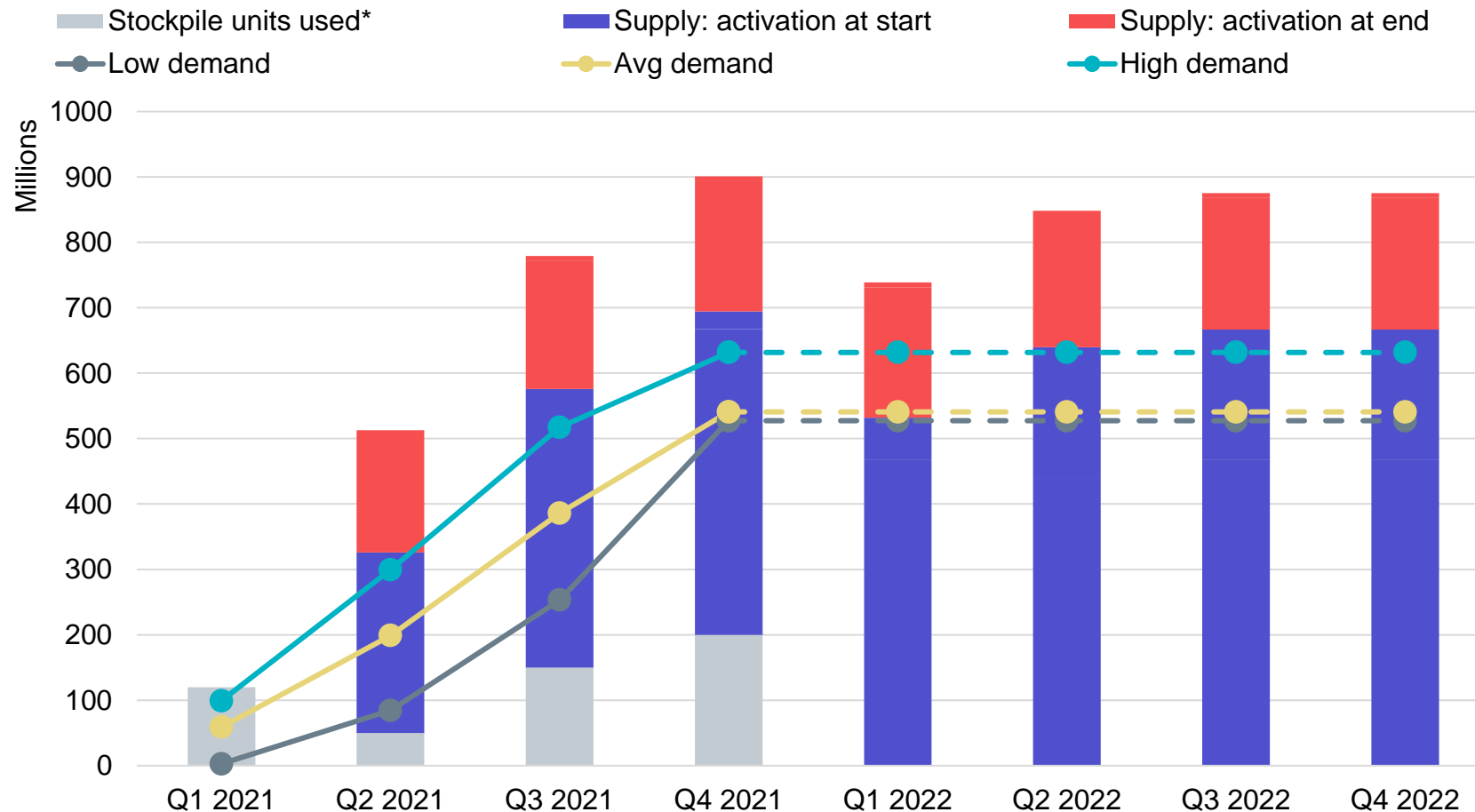
- 520 million syringes are estimated in the COVID-19 syringe stockpile
- Strategic use of the syringe stockpile could meet high demand forecast using only syringes with AD activation at the start of injection through 2021.

*Assuming stockpile of 520 million AD syringes is consumed as needed to meet demand through 2021.

**Supply data shown assumes 70 percent of COVID-19 syringe supply is available to the COVAX AMC countries.

***Demand forecasts as of Dec 1 2020.

Additional investment could further supply by adding new lines



Key findings:

- Graph assumes investment in additional production lines is made in Q1 2021.
- With additional investment in new production lines, activation at the start syringes could be used in most years in 2022 and beyond.

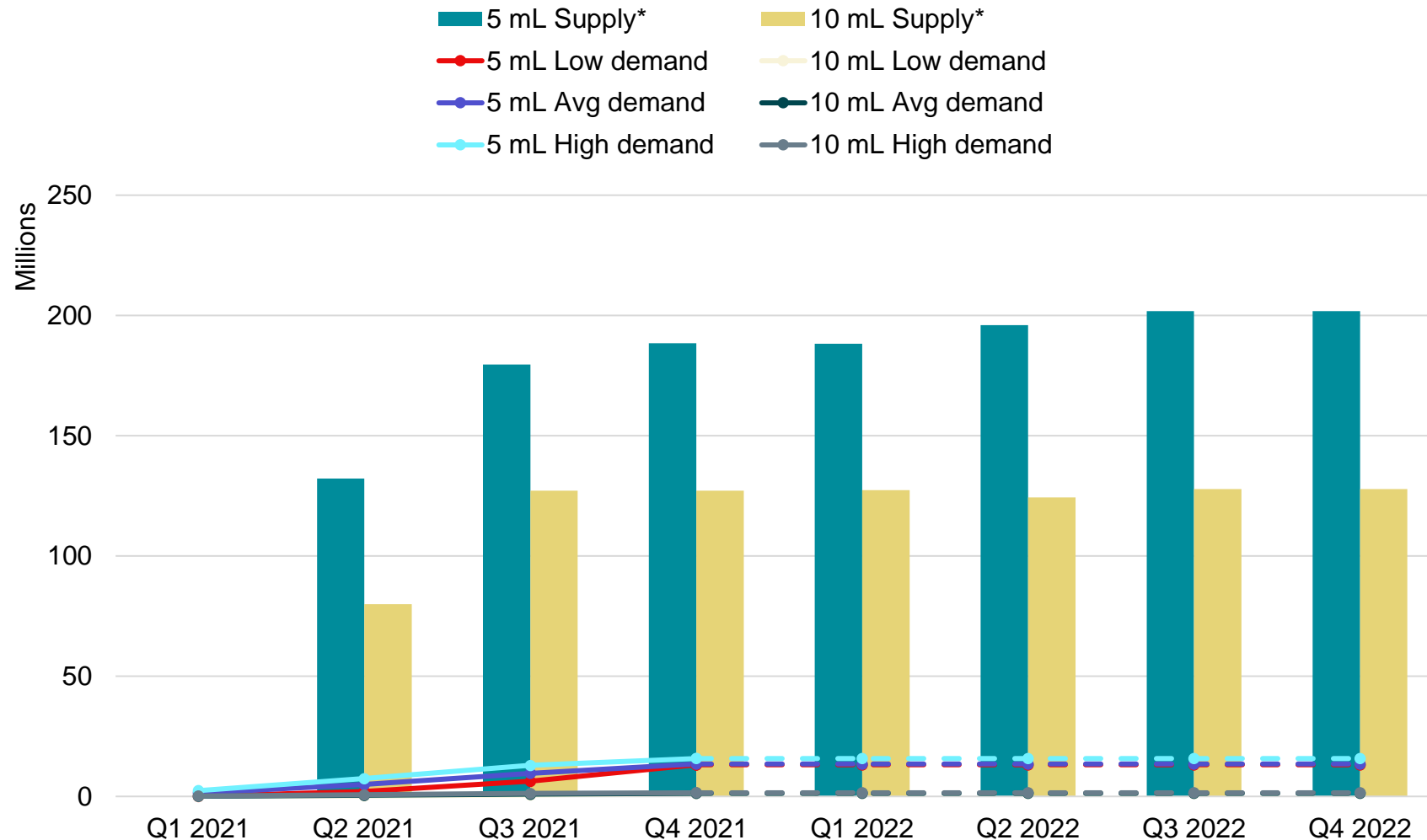
*Assuming stockpile of 520 million AD syringes is consumed as needed to meet demand in 2021.

**Supply data shown assumes 70 percent of COVID-19 syringe supply is available to the COVAX AMC countries.

***Assuming investment is made in Q1 2021. Additional supply available from investment varies based on time of investment.

****Demand forecasts as of Dec 1 2020.

RUP syringe gap analysis



Key findings:

- A relatively small number of RUP syringes are anticipated to be needed for COVID-19 vaccines, as most vaccine candidates are liquid and in multidose vials.
- RUP syringe supply capacity significantly exceeds potential demand in all scenarios.

*Supply data shown assumes 70 percent of COVID-19 syringe supply is available to the COVAX AMC countries.

**Demand forecasts as of Dec 1 2020.

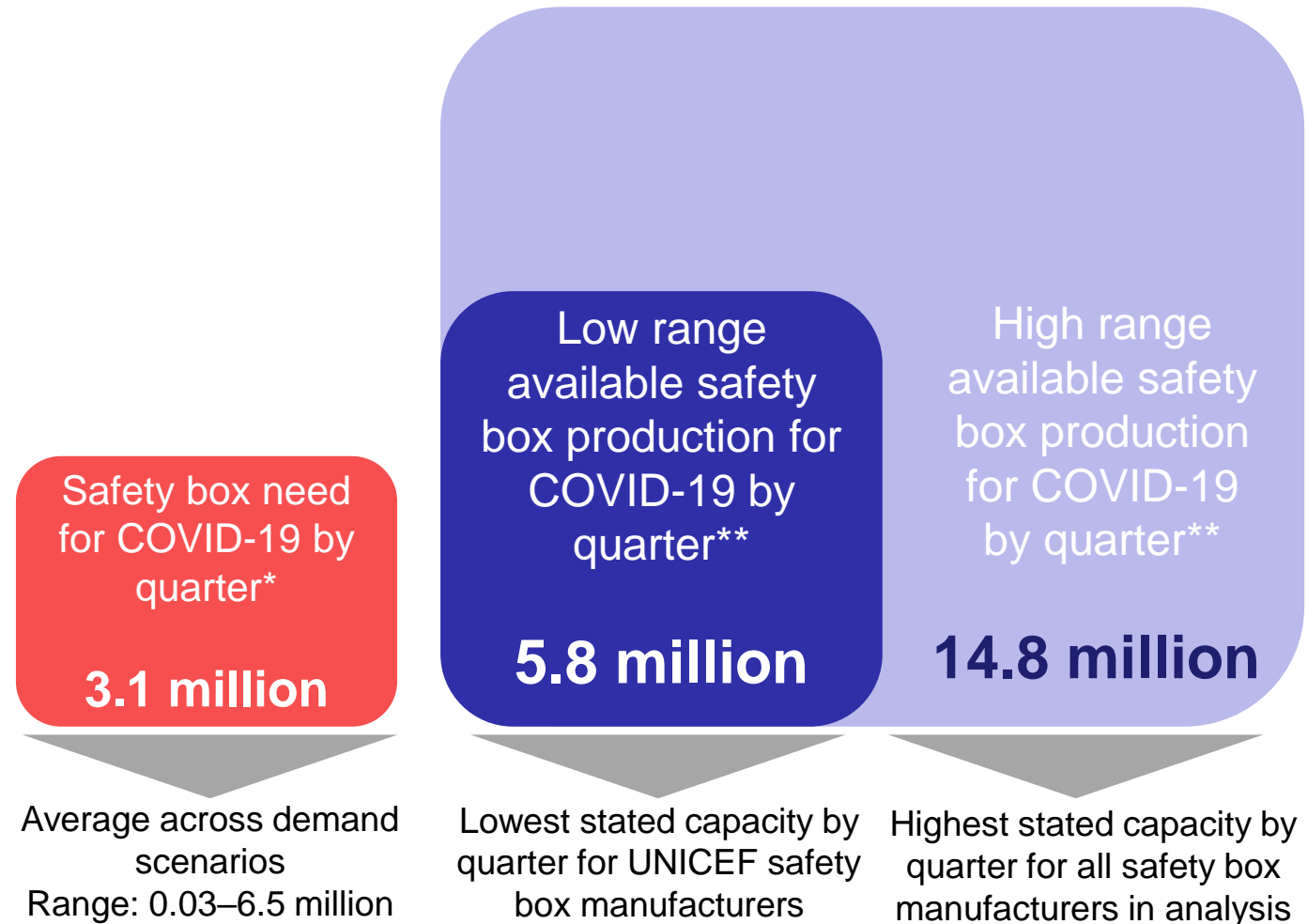
Pre-COVID-19 safety box production and market share by manufacturer highlights few players based on primary research

Quarterly units produced:

3,454,300

Safety box needs far exceeded by supply and can be fully met by UNICEF safety box manufacturers

- Manufacturers can easily scale production with minimal investment or advance notice.
- Most manufacturers could double, if not triple production within three months.
- UNICEF safety box manufacturers could meet high forecasted COVID-19 demand across all quarterly estimates starting in Q1 2021.



Non-standard dose volume AD syringes

- There are currently no WHO-prequalified 0.3 mL AD syringes (dose volume for Pfizer/BioNTech vaccine).
- Informal questioning of largest manufacturers suggests it is possible to produce tens of millions of 0.3 mL AD syringes by the end of Q1 2021 if orders are placed immediately. UNICEF tender is in process.
- WHO PQ approval is a key timeline risk (review will be expedited if dossiers are complete).
- Rapid coordination between UNICEF, syringe manufacturers, and WHO PQ will be critical to ensure syringe supply when vaccine doses are available; air transport essential.
- Production of 0.3 mL syringes will reduce 0.5 mL production capacity by an equal amount (same lines used).
- Potential for need for non-0.5 mL AD syringes for other COVID-19 vaccines should be closely monitored (e.g. reduced dose delivery of AstraZeneca vaccine) and syringe procurement adjusted accordingly.



PharmaJet disposable syringe jet injector



PharmaJet Stratis®



PharmaJet Tropis®

- PharmaJet's Stratis (0.5 mL dose for intramuscular/subcutaneous delivery) and Tropis (0.1 mL dose for intradermal delivery) disposable-syringe jet injectors are WHO prequalified and use autodisable needle-free syringes.
- Use in large-scale vaccination campaigns (fIPV in Pakistan) with good acceptability.
- Jet injection of nucleic acid vaccines has been demonstrated to enhance immunogenicity compared to needle injection.
- Device cost can be offset by dose-sparing for some vaccines.
- Manufacturing scale up from current production volumes in progress.
- Eighteen COVID-19 vaccine partnerships in development; 4 in Phase I trials and 1 in Phase II.

Prefilled delivery devices

CPAD device

A CPAD device is **compact, pre-filled, and autodisable** in order to meet needs in low-resource settings (in contrast to traditional glass prefilled syringes).

Existing technologies:

- BD Uniject: The only CPAD device on the market (requires specialized filling equipment).



PATH

- Injecto easyject: Based on a polymer-prefilled syringe bell.



PATH

BFS prefilled devices

Blow-fill-seal (BFS) is a method of producing liquid-filled containers that are formed, filled, and sealed in a continuous, automated system with the following characteristics:

- High-production volumes
- Flexible container design
- Low-cost process

For parenteral products, BFS containers can be formed as ampoules, vials, or prefilled injection devices.

Currently no BFS device is a CPAD (they all lack an AD feature).



Photo: Brevetti Angela

Angela Brevetti prefilled injection device



Photos: Apiject

Apiject prefilled injector



Apiject + COVID-19

Apiject has received ~\$150 million in funding from the US government to support the domestic COVID-19 response. Funded activities include:

1. Design finalization and regulatory 510(k) filings for a BFS container with a separate, user-attached needle hub.
2. Retrofitting of a domestic BFS facility to biosafety level 2 (BSL-2) to allow for vaccine filling.
3. Capacity for production scale filling of 100 million units by end of 2020.

Intact Solutions multidose pouches

Intact Solutions' 200- and 400-dose pouch technologies are under evaluation by CEPI as an alternative packaging option for COVID-19 vaccines, with the aim of expanding production capacity beyond the limitations of glass vials, minimizing cold chain volume, and speeding delivery. Two pouch options are being advanced, and **neither is compatible with fixed-needle AD syringes**.

Pouch version	Delivery options	Notes
 <p>Luer port pouch</p>	Conventional luer needle and syringe	<ul style="list-style-type: none"> Not aligned with policies on use of AD syringes for immunization.
	RUP syringe with removable luer needle	<ul style="list-style-type: none"> Mitigates but does not eliminate risk of reuse of injection device. Prequalified syringe suppliers have stated they are able to produce fixed-dose 0.5 mL RUP syringes with removable needle (not a currently supplied product) or a similar price as standard RUP syringe.
 <p>Multidose syringe pouch</p>	Conventional needle	<ul style="list-style-type: none"> Widely produced and inexpensive. Risk of inadvertent/intentional reuse of needle, and needlestick injury due to need to remove used needle from reusable syringe.
	SIP needle	<ul style="list-style-type: none"> Commercially available. Mitigates but does not eliminate risk of reuse.
	AD/SIP needle	<ul style="list-style-type: none"> Strongly preferred by stakeholders to minimize risk of needle reuse and needlesticks. Not a commercially available technology. Design concepts available from Intact Solutions and the Stevanato Group. Increased cost and time required for development and scale up.

Risks include demand uncertainty and additional warehousing needs



Demand uncertainty and timing

- Manufacturers concerned with **demand dropping off**, especially if they have added lines or purchased new machinery to meet COVID-19 demand.
- **Purchase commitments** expected but they have only been realized primarily for UNICEF to date.
- **Lack of clarity on vaccine candidates, dosage, and syringe requirements** create uncertainty for syringe needs.
- Lack of confidence in vaccine supply estimates and country vaccination implementation timelines.
- **Limited transparency in potential demand from non-COVAX countries**, especially UMIC.



Material constraints

- Some concern around specific materials (syringe molds, needles) if there was a large surge in orders.
- Pricing affected by increased duty/customs costs, shipping for imported raw materials.



Logistical challenges

- **Shipping lead times can be out of manufacturers' control** and could create delays.
- Air travel a constraint since the start of the COVID-19 pandemic (typically only used if urgency for an order).



Warehousing needs

- Limitations in storage capacity (many manufacturers can only hold supply for one month).
- Increasing production may require expanding warehousing, repurposing other space, or renting additional space.

Information sharing and robust planning is critical for mitigating risks from uncertainties and constraints

Identified risk

Proposed mitigation



Demand uncertainty and timing

- Provide more transparency around market to manufacturers, such as this analysis with confidential information removed.
- Communicate updated information around vaccine candidates, dosing, and other considerations to all stakeholders.



Material constraints

- Potential to control material constraints through purchasing materials in advance.
- Develop purchase order terms and conditions to help make procurement processes more efficient.



Logistical challenges

- Schedule out when deliveries are needed with advance notice based on shipping times to geographic regions.



Warehousing needs

- Determine whether warehousing is needed in-country and plan for additional storage (i.e., stockpiling in centralized locations or renting space in-country).
- Plan for additional budget needed to secure additional space.

Estimated supply meets COVID-19 vaccination needs in all demand scenarios if AD syringes with activation at start and end of injection are used

Available production of start and end of injection AD syringes meet all demand scenarios.

- Existing stockpile could be used to close the gap in demand for start-activation syringes for 2021.
- Additional investment may be required to meet long-term needs if COVID-19 vaccine distribution stays high in future years and if only start of activation syringes are desired.

Available RUP and safety box production far exceeds demand.

- UNICEF safety boxes bundle suppliers can meet all demand scenarios.

Efforts may be constrained by shipping times and warehousing.

- International shipping estimates range from 10–70 days, but may not be influenceable.
- For many manufacturers, existing warehousing is not sufficient to meet sustained surges in production and will require planning for additional storage.

Market uncertainty can be mitigated with targeted communication and contracting

- Manufacturers used to a relatively stable market face new demand uncertainties, but can respond with lead time.
- Advanced purchase commitments could provide more visibility to the market needs.

Limitations for this analysis

1. Manufacturing self reported creating potential bias.
2. Only some manufacturers provided information on their ability to add manufacturing lines if additional investment was made.
3. Unclear precise volume of AD syringes that will go to upper middle- and high-income countries.
4. Visibility of existing country stockpiles is limited by lack of information on downstream stocks and scheduled deliveries for campaigns.
5. Potential reductions in routine immunization may create surpluses in syringe supply.
6. Potential bilateral agreements between AD syringe-using countries and vaccine manufacturers may result in underestimation of AD syringe demand.
7. Estimated number of vaccine doses, which are shifting as new vaccine information is obtained, are used as a proxy for syringe demand

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Appendix



Definitions

Auto-disable (AD) syringe: disposable delivery device with a non-removable needle that automatically (passively) disables after a single, fixed-dose injection. Depending on the design, the auto-disable feature may be a clip lock or plunger lock/break, which is activated at the start, middle, or end of the injection. AD syringes are designed to prevent disease transmission through a mechanism that blocks syringe reuse. UNICEF exclusively procures AD syringes for immunizations, typically in 0.1–0.5 mL sizes.

Reuse prevention (RUP) syringe: disposable delivery device that can deliver variable doses with a mechanism to prevent reuse. The reuse prevention mechanism can be activated automatically or manually. RUP syringes are recommended for reconstituting vaccines and delivery of curative injections, typically in 2–10 mL sizes.

Safety boxes: containers for used syringe and needle disposal. Boxes should be water resistant and puncture resistant. Safety boxes can be purchased with syringes to ensure enough boxes to dispose of syringes, often referred to as bundling. A typical 5L box is suitable for disposing 100 syringes depending on the syringe size and other conditions. Other sizes include 2.5 L, 10 L, and 15 L.

Vaccine reconstitution: the process by which lyophilized (freeze-dried) vaccines are combined with a diluent to make a liquid formulation prior to administration. Reconstitution requires a reconstitution syringe and needle, in addition to a delivery syringe for administration.

World Health Organization (WHO) prequalified products: a product that has successfully undergone the WHO prequalification process, ensuring they meet global standards for quality, safety, efficacy, and programmatic suitability. WHO develops and maintains a list that meet these standards and can be procured by UN agencies.

Primary market research topics included probing on three supply scenarios

Supply scenarios

- **Pre-COVID-19 production:** How many **syringe X** units did you manufacture in the most recent quarter?
- **Future available production with existing manufacturing lines:** Are you able to increase supply of **syringe X**, either by repurposing existing manufacturing lines or by increasing production on the existing/planned manufacturing lines? With your existing/planned manufacturing lines, what is the theoretical increase in number of units of **syringe X** that you could manufacture if there was demand?
- **Future available production with new investment:** Would a new purchase commitment enable you expand the number of manufacturing line(s) within your existing infrastructure to produce **syringe X**? What is the theoretical quarterly number of units of **syringe X** that you could manufacture on the new manufacturing line(s)?

COVID-19 production

- For *How many **syringe X** units did you manufacture in the most recent quarter?* What percentage are for COVID-19 vaccine use? What percentage are for non-COVID-19 vaccine use?
- For *How many **syringe X** units did you manufacture in the most recent quarter?* What percentage are for COVID-19 vaccine use? Have customers already procured or submitted purchase orders for **syringe X** for COVID-19 vaccine use?

Considerations

- What considerations do you have when deciding whether to increase production?
- In what month and year would you be able to start increasing supply of **syringe X** using your existing/planned manufacturing lines if demand was articulated on January 1, 2021?

Warehousing

- Are there plans for expansion of holding / warehousing for **syringe X** for COVID-19 vaccine needs?

Shipping times

- What are your approximate shipping times in number of months to each of the following regions? (North Africa, sub-Saharan Africa, South Asia, Central Asia, East Asia, Americas, Europe).

Note: Subset of research topics; not comprehensive.

Full WHO prequalified list includes a range of options for AD and RUP immunization-related products

AD syringes

46 distinct WHO prequalified AD syringes

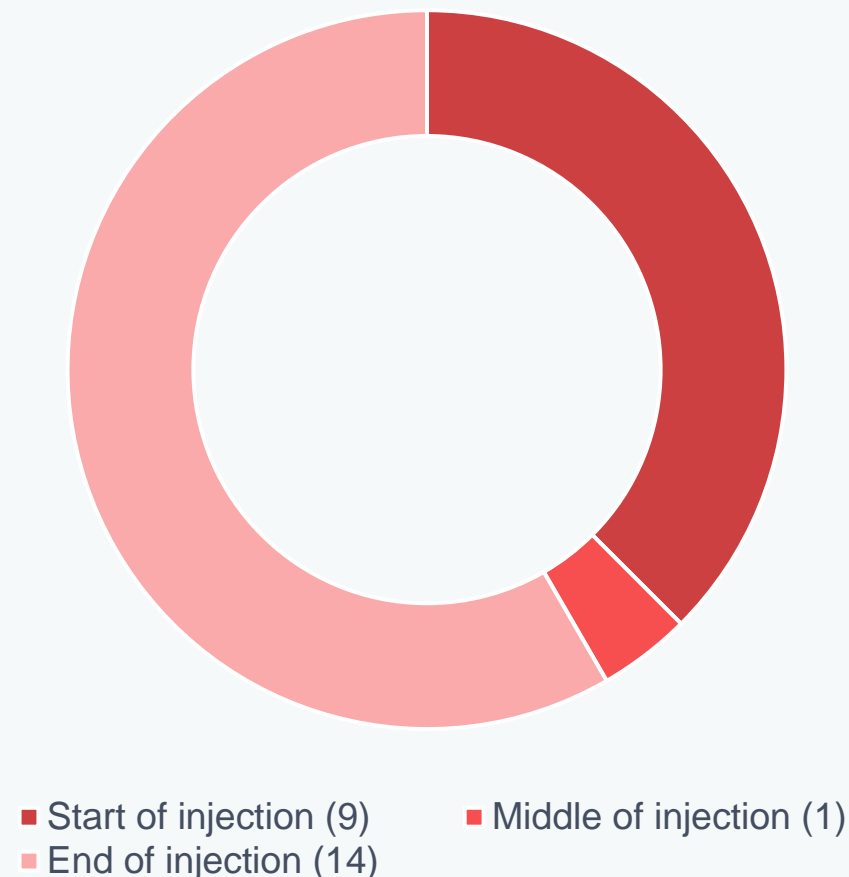
- Fill volumes: 0.5 mL, 0.25 mL, 0.1 mL, 0.05 mL
 - 52 percent are 0.5 mL (24 of 46 syringes)
- 19 manufacturers of AD injection devices
 - 18 manufacturers make 0.5 mL needle and syringes
 - 1 manufacturer (PharmaJet) of disposable-syringe jet injectors (0.1 mL and 0.5 mL)
- 11 AD syringes have UNICEF LTA
 - 7 syringes (from 6 manufacturers) are 0.5 mL with AD mechanism at start of injection

RUP syringes

104 distinct WHO prequalified RUP syringes

- Fill volumes: 20 mL, 10 mL, 5 mL, 3 mL, 2 mL, 1 mL
 - 37 percent are 5 mL or 10 mL (38 of 104 syringes)
- 21 manufacturers
 - All manufactures make 5 mL or 10 mL fill volume syringes
- 10 syringes have UNICEF LTA
 - 5 manufacturers

AD syringe mechanism (0.5 mL)



The AD syringe market represents 0.2 percent of the total global syringe market, showing consistent growth before COVID-19

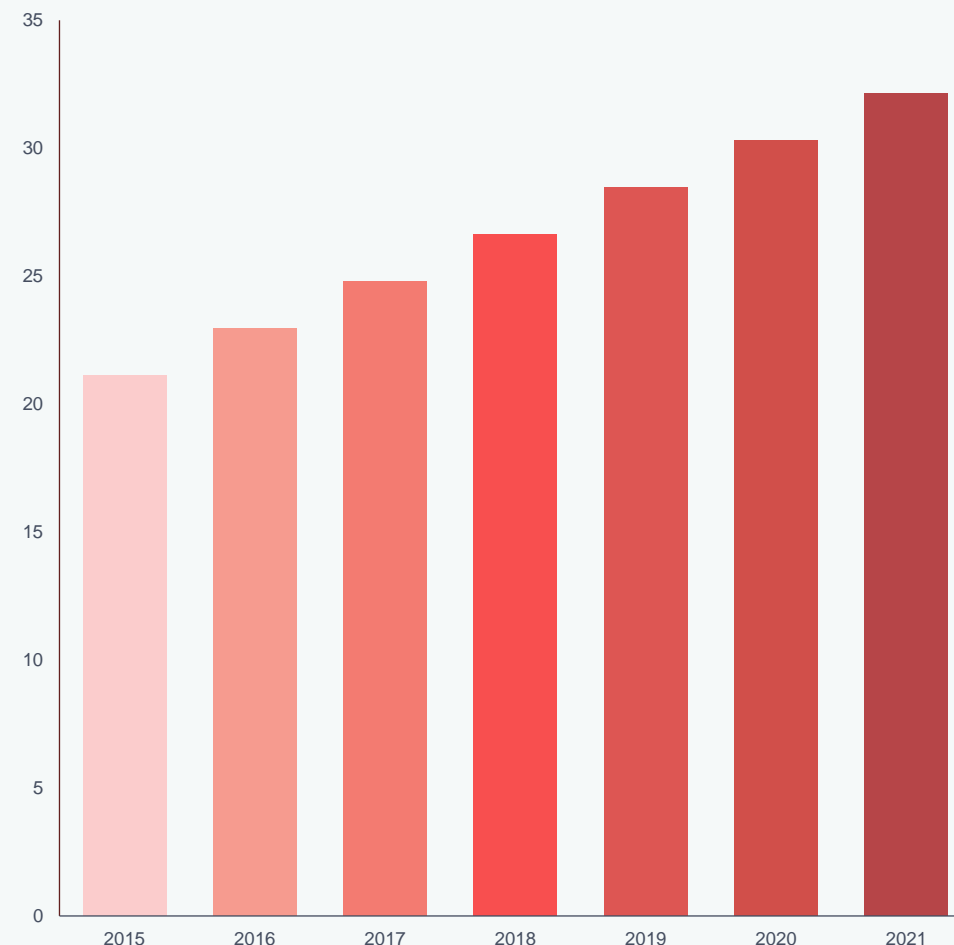
Pre-COVID-19, global syringe market expected to be valued at USD 16.07 billion by 2021.

- Expected compound annual growth rate **of 8.7 percent** between 2015 and 2021.
- Potential for this compound annual growth rate to increase in light of COVID-19 pandemic and mass global vaccination efforts.

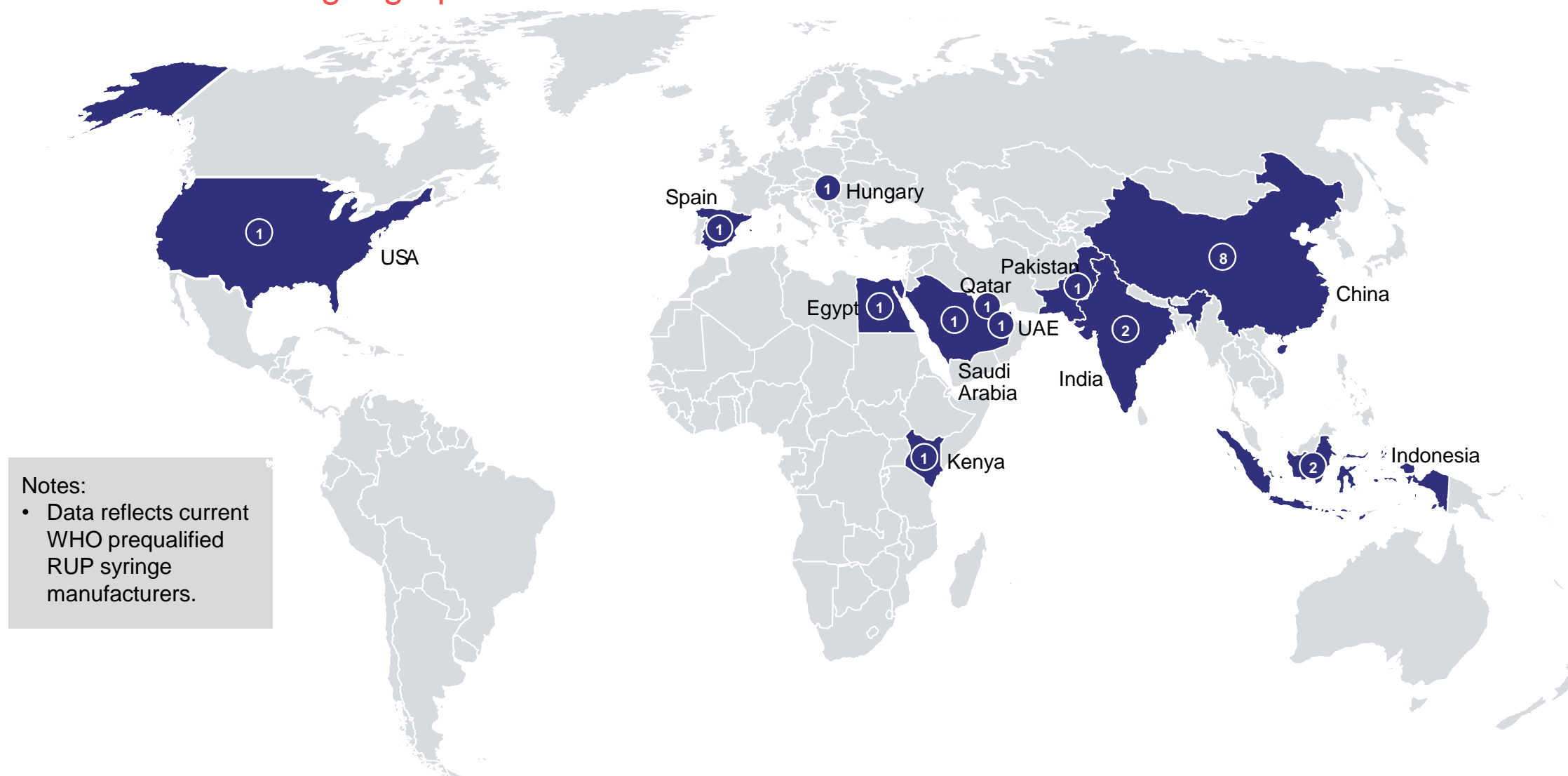
The AD syringe market segment represents only 0.2 percent of the total syringe market, but accounts for a significantly higher percentage of syringes in LMIC countries.

WHO estimates **16 billion injections** are administered every year.

Market value of AD syringes
(in USD millions)



RUP 5 mL and 10 mL syringes are manufactured and warehoused predominantly in low- and middle-income geographies



Notes:

- Data reflects current WHO prequalified RUP syringe manufacturers.

Abbreviations

AD	autodisable
AMC	Advance Market Commitment
BFS	blow-fill-seal
COVAX	Covid-19 Vaccines Global Access
COVID-19	Coronavirus disease 2019
CPAD	compact, pre-filled, autodisable
Gavi	Gavi, The Vaccine Alliance
HICs	high-income countries
LMICs	lower-middle income countries
LTA	long-term agreement
PAHO	Pan American Health Organization
RUP	reuse prevention
SIP	sharps injury prevention
UMIC	upper middle-income countries
UN	United Nations
UNICEF	United Nations Children's Fund
US	United States
WHO	World Health Organization

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