

## GLOBAL MARKET STUDY

### SEASONAL INFLUENZA VACCINE

#### Key Takeaways

- WHO provides recommendation on the composition<sup>1</sup> of **seasonal influenza vaccine** semi-annually due to changes in the circulating virus and new vaccines are manufactured and made available for administration to targeted populations.
- Seasonal influenza demand is stable and **highly concentrated in high- and upper-middle income countries**, which together consume over 95% of seasonal influenza vaccines. Only 27 (34%) countries classified by the World Bank as low- or lower-middle-income reported having a policy for seasonal influenza vaccination.
- The seasonal influenza vaccine supplier base is large, **but more than 85% of annual volumes are supplied by seven producers**. Four manufacturers produce improved seasonal influenza vaccines<sup>2</sup>, which comprise only 10% of available influenza vaccines.
- Demand for seasonal influenza vaccines is forecasted to **increase by ~10% in the next 10 years** and there is significant potential to increase seasonal influenza vaccine use – particularly in lower-middle and low-income countries; though financing and prioritization over other health interventions would be required. Limited investment in health workers and maternal vaccination could carry outsized health and programmatic benefits.
- **Supply of seasonal influenza vaccines is sufficient to meet current and forecasted country demand**, except in the event of multiple manufacturers exits, which are considered unlikely. In the event of demand from the lowest income countries, country-specific availability and suitability of vaccines would need to evolve.
- Vaccines under development with faster manufacturing processes could potentially provide improvements over available vaccines and large increases to available supply for commercialisation in the medium term.
- In the short term, **limited access risks** exist due to the regulatory and implementation complexities necessitated by WHO's recommended removal of the B/Yamagata strain from quadrivalent vaccines. Increased coordination will be necessary to ensure successful transition from QIV to TIV, considering the needs and constraints of Member States, regulatory agencies, and industry.

#### QUICK STATS

##### NUMBER OF VACCINE PRODUCTS

122

##### NUMBER OF VACCINE PRODUCTS WHO PRE-QUALIFIED

20

##### TOTAL NUMBER OF BULK PRODUCERS (MANUFACTURERS)

30

##### TOTAL NUMBER OF FILL/FINISH PARTNERS

12

##### 2024 ESTIMATED GLOBAL SUPPLY

1.2 BILLION TRIVALENT EQUIVALENT DOSES\*

##### 2024 ESTIMATED GLOBAL DEMAND

850 M DOSES

##### MEDIAN 2022 ADULT QUADRIVALENT PRICE PER DOSE

US\$ 4.72 (LMIC) TO US\$ 10.67 (HIC)

##### MEDIAN 2022 ADULT TRIVALENT PRICE PER DOSE

US\$ 3.54 (LMIC) TO US\$ 3.08 (HIC)

\* All ASC has been standardized to trivalent-equivalent doses to enable a dose-to-dose comparison and shared manufacturing capacity between quadrivalent and trivalent doses. It is assumed that each quadrivalent dose is equivalent to 1.25 trivalent doses.

#### Context and Rationale

In 2022, following SAGE (Strategic Advisory Group of Experts on Immunisation) advice, WHO updated its recommendation for seasonal influenza vaccine use<sup>3</sup>. The updated recommendations state that all countries should consider implementing seasonal influenza immunisation programmes and that the following target

groups be considered for vaccination: health workers, individuals with comorbidities and underlying conditions, older adults, and pregnant women<sup>4</sup>. Countries may consider vaccination of additional populations such as children and may prioritise groups based on the local context<sup>5</sup>. The use of seasonal influenza vaccines can contribute to strengthening life-course immunisation as called

<sup>1</sup> The virus strains included in the vaccines, based on evidence of strains circulating and infecting humans.

<sup>2</sup> Any influenza vaccine designed to provide improvement over current, standard dose influenza vaccines in terms of durability, efficacy, breadth of protection, or programmatic suitability.

<sup>3</sup> WHO position paper on seasonal influenza vaccines – May 2022. Weekly Epidemiological Record, 2022, vol. 97, 19 [full issue] (<https://www.who.int/teams/immunization-vaccines-and-biologicals/policies/position-papers/influenza>; accessed 20 November 2023)

<sup>4</sup> These four populations recommended for seasonal influenza vaccination are referred to as “priority groups”.

<sup>5</sup> New influenza disease burden data is expected to be made available by 2025-2026 which may inform updated target group recommendations.

for in the Immunisation Agenda 2030 (IA2030) and is a critical component of preparedness for an influenza pandemic, as indicated in WHO's Global Influenza Strategy, 2019-2030. National seasonal influenza vaccination programmes able to achieve high coverage in all recommended populations can help ensure that manufacturing capacity and capabilities are available and that appropriate systems are in place to facilitate vaccine deployment in the event of an influenza pandemic<sup>6</sup>.

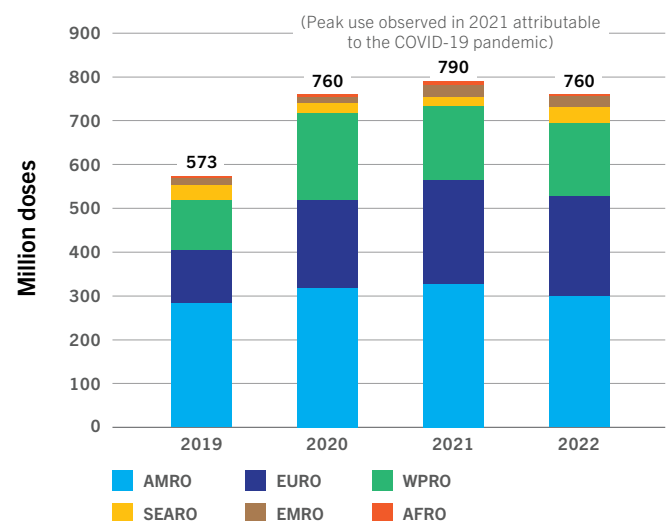
The increased focus on pandemic preparedness following the COVID-19 pandemic and anticipated changes to the seasonal influenza vaccine market necessitates a deeper understanding of market dynamics to support global, regional, and country decision-making. Numerous influenza vaccines are being developed which can provide improvements over available seasonal influenza vaccines. The impact and public health value of current and improved seasonal influenza vaccines will be summarised in WHO's Full Value of Improved Influenza Vaccine Assessment and will help to inform future decisions on influenza vaccine policy and use. Evaluation of market dynamics plays a key role in this assessment. This study provides an updated understanding of global trends and drivers of seasonal influenza vaccine supply and demand to enable equitable access to seasonal influenza vaccines for all countries, across all regions and income groups.

## Market Background

The existence and scope of national policies guiding influenza vaccine use are highly variable. As of November 2023, 123 (63%) countries report having an influenza vaccination policy through the WHO/UNICEF Joint Reporting Form (JRF). This includes 96 (85%) countries classified by the World Bank as high- (HIC) or upper-middle-income countries (UMIC).<sup>7</sup> Among countries with a policy, 74 (60%) recommend vaccination of all WHO priority groups, while 41 countries (33%) report having policies which extend beyond WHO recommendations to cover the entire population. By contrast, only 27 (34%) of low- (LIC) and lower-middle income countries (LMIC) have a policy recommendation to support public financing, procurement, or use of seasonal influenza vaccines, highlighting the uneven use of seasonal influenza vaccines in different income groups and therefore opportunity for demand growth.

This results in high concentration of seasonal influenza vaccine consumption. In 2022, HICs and UMICs consumed 97% of global seasonal influenza vaccine produced and 92% of consumption was in the Region of the Americas, European Region, and Western Pacific Regions combined<sup>8</sup> (Figure 1). Vaccine use is also concentrated in only five countries that together account for 55% of global volumes. Quadrivalent vaccines (QIV) formulated for adults were 65% of global seasonal influenza vaccine consumption<sup>9</sup>. The use of improved seasonal influenza vaccines remains limited and is concentrated in HICs.

FIGURE 1: SEASONAL INFLUENZA VACCINE VOLUME BY WHO REGION, 2019 - 2022



The constant evolution of influenza viruses<sup>10</sup> necessitates bi-annual reformulation of vaccines to match circulating influenza viruses. To respond to the seasonality of influenza transmission, the timing of manufacturing and vaccination is different to address the needs of the northern and southern hemispheres resulting in semi-annual cycles of supply and demand. Seasonal influenza vaccines formulated with northern hemisphere strains made up 64% of global volumes in 2022, vaccines using southern hemisphere formulation comprised 20% of global volumes, while 15% of global volumes were used in countries which use both northern and southern hemisphere formulations<sup>11</sup>. Since 2012, seasonal influenza vaccines have consisted of two influenza A strains and one influenza B strain in trivalent vaccines (TIV), with the addition of the B/Yamagata strain in QIV. The two most common seasonal influenza vaccines are 1) inactivated vaccines produced in eggs or cell cultures and 2) live attenuated vaccines (LAIV) which comprised ~98% and ~2% of 2022 seasonal influenza vaccine volumes, respectively.

Globally, bulk influenza vaccine is produced by 30 manufacturers, seven of them are responsible for >85% of global supply, with the remainder serving primarily local markets. The headquarter location of bulk producers are diverse, but 75% are in Europe and Asia (Figure 2). Seven of the ten highest volume manufacturers have registered their vaccines and provided vaccine to more than 10 countries (range 10 – 72) in 2022<sup>12</sup>. Nineteen manufacturers supply vaccines to both hemispheres, while ten supply only northern hemisphere formulated doses, and one supplies only southern hemisphere formulated doses. As of 2022, sixteen

6 Global influenza strategy 2019-2030. Geneva: World Health Organization; 2019. Licence: CC BY-NC-SA 3.0 IGO. Cataloguing-in-Publication (CIP) data. CIP data are available at <http://apps.who.int/iris>

7 World Health Organization, WHO/UNICEF Joint Reporting Form (for download). Cited 20 November 2023. Available at <https://immunizationdata.who.int/listing.html?topic=&location=>

8 WHO MI4A dataset

9 WHO MI4A dataset

10 Recommendations announced for influenza vaccine composition for the 2023-2024 northern hemisphere influenza season. Available at <https://www.who.int/news/item/24-02-2023-recommendations-announced-for-influenza-vaccine-composition-for-the-2023-2024-northern-hemisphere-influenza-season>

11 WHO MI4A dataset

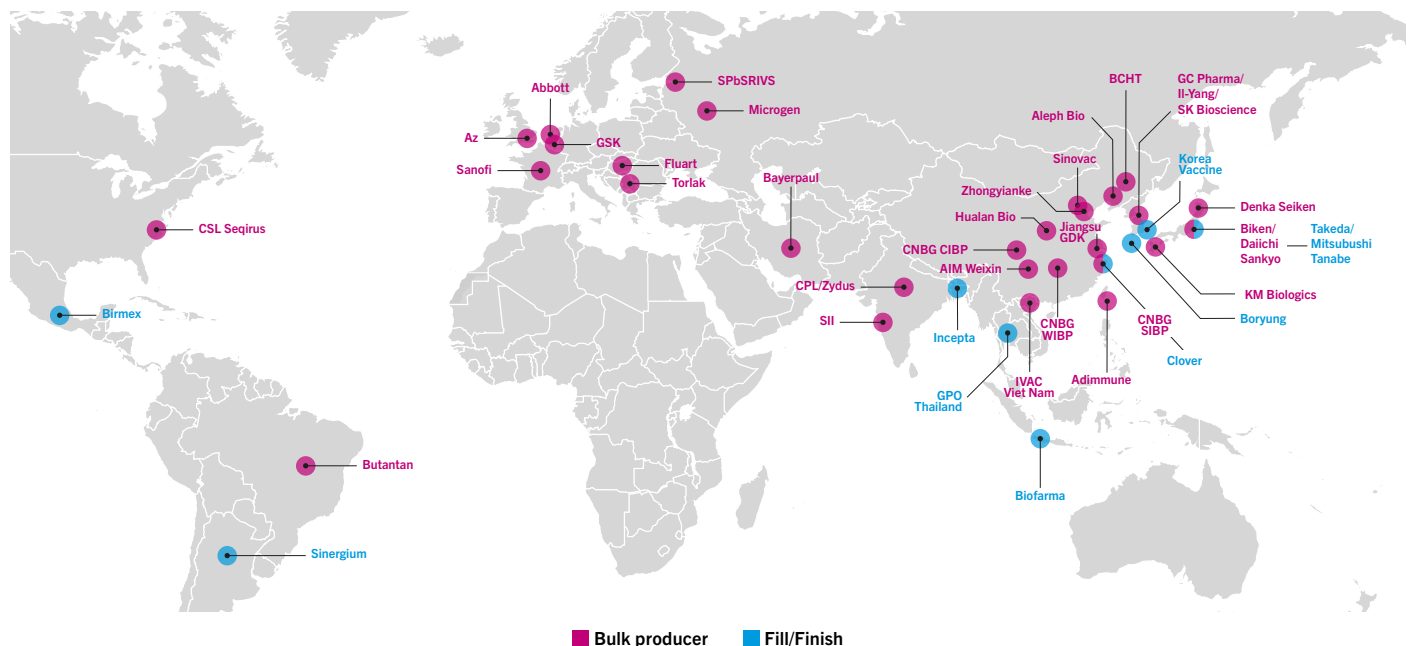
12 WHO MI4A dataset

manufacturers supply both TIV and QIV, five supply only TIV and nine supply only QIV. Of note, the production capabilities of six manufacturers were supported by a WHO Technology Transfer Initiative<sup>13</sup>.

There are at least 122 seasonal influenza vaccines on the market which are produced by 42 companies, 12 of which perform only filling & finishing of the bulk vaccine. Twenty vaccines produced

by ten manufacturers are WHO-prequalified. Improved vaccines, including those containing adjuvants, higher-antigen content or those made with a recombinant antigen, are used in some countries for specific target groups. Only 10% of available vaccines are considered improved and they are supplied by four bulk producers.

FIGURE 2: MAP OF SEASONAL INFLUENZA VACCINE MANUFACTURERS HEADQUARTERS LOCATIONS



In September 2023, recommendations from WHO stated that “the inclusion of a B/Yamagata antigen as a component of influenza vaccines is no longer warranted, and every effort should be made to exclude it as soon as possible.”<sup>14</sup> This recommendation has the potential to alter current market dynamics as it is expected that QIV may be phased out with a reversion to the exclusive use of TIV. National regulatory agencies and vaccine manufacturers will play a key role in the implementation of WHO’s recommendations

### Global Demand (Programmatic Doses Requirements)

A global demand forecast for seasonal influenza vaccine has been developed for the period 2023-2034 based on historical procurement data and the latest available information regarding seasonal influenza vaccine use in countries. A base-case scenario was developed based on countries’ current national influenza vaccination policies and vaccination coverage levels per target group. The scenario assumes that: (1) existing national influenza vaccination policy recommendations will continue unchanged; (2) no new countries will adopt and implement

seasonal influenza vaccination programmes; (3) coverage in the target groups remain constant over the forecasted period.

In this scenario, global seasonal influenza vaccine programmatic dose requirements (PDR) will total ~850M doses in 2024. This is an increase from historical consumption due to policy changes made in 2022-2023 in high-volume countries, including China. Demand is projected to slowly increase between 2024 and 2034, reaching ~920M doses by the end of the period, driven by forecasted growth of the older persons population, one of WHO’s priority groups. With no expected expansion in seasonal influenza vaccine policies and use in LMIC and LICs, PDR is anticipated to remain concentrated in HICs and UMICs (~95% by the end of the forecasted period).

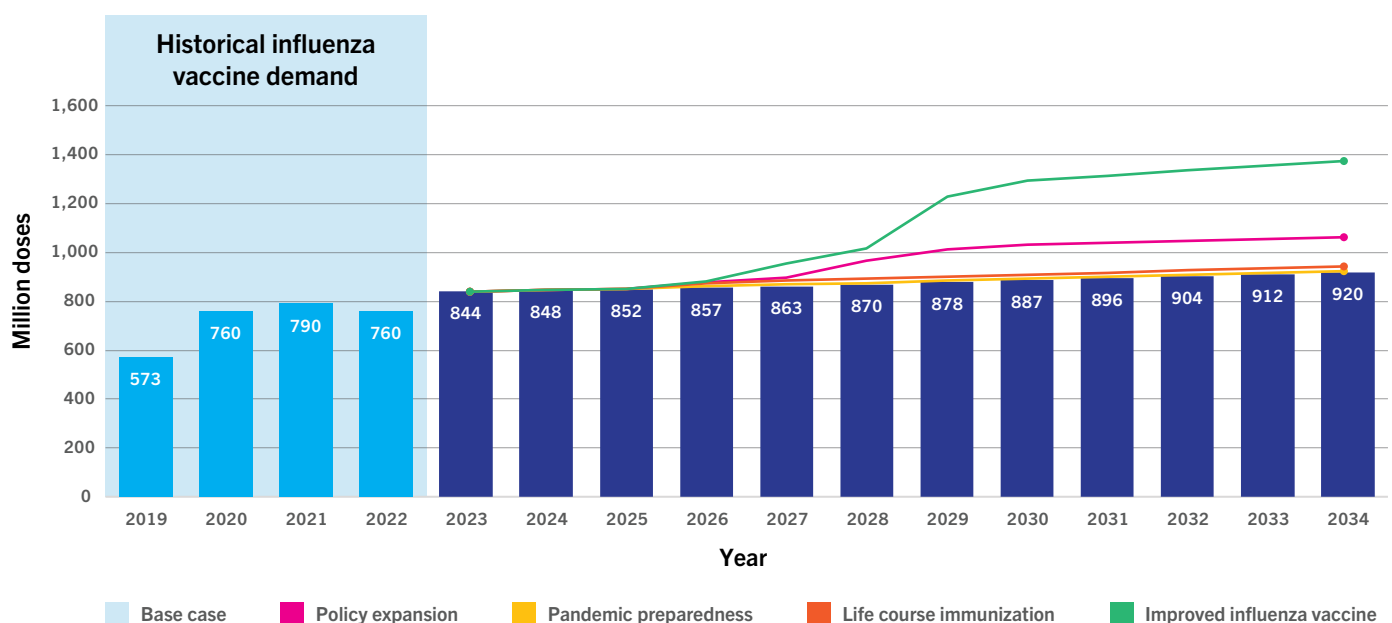
To assess the potential evolution of seasonal influenza vaccine demand under different programmatic and policy conditions, including increased use in LICs and LMICs, different scenarios have been modelled (Figure 3). Each of the scenarios build on top of the forecasted demand in the base scenario.

13 Christopher Chadwick, Martin Friede, Ann Moen, Claudia Nannei, Erin Sparrow, Technology transfer programme for influenza vaccines – Lessons from the past to inform the future, Vaccine, Volume 40, Issue 33, 2022, Pages 4673-4675, ISSN 0264-410X, <https://doi.org/10.1016/j.vaccine.2022.06.057>.

14 Recommended composition of influenza virus vaccines for use in the 2024 southern hemisphere influenza session. Available at: Recommendations announced for influenza vaccine composition for the 2023-2024 northern hemisphere influenza season. Available at <https://www.who.int/news/item/24-02-2023-recommendations-announced-for-influenza-vaccine-composition-for-the-2023-2024-northern-hemisphere-influenza-season>

- The **pandemic preparedness scenario** assesses the impact of the seasonal influenza vaccination of health workers in all countries; PDR in the short, medium, and long term are comparable to the base scenario due to the small size of the health worker population when compared to the existing dose requirements for seasonal influenza vaccine.
- The **life course vaccination scenario** evaluates an evolution of the influenza programme in which all countries vaccinate pregnant women. The PDR required to support this change is marginally higher (~20M doses per year) than the base scenario.
- The **policy expansion scenario** provides insight into the implications of expanded use of seasonal influenza vaccines in HICs and UMICs should they all recommend and vaccinate all WHO priority groups, in addition to groups vaccinated in the base scenario. This scenario results in the second-largest increase in PDR among the evaluated scenarios, with required doses stabilising at ~1 billion in 2029.
- The **global priority group vaccination scenario** simulates the availability of a vaccine which meets the WHO Preferred Product Characteristics (PPC) for improved influenza vaccines, which results in all countries vaccinating all WHO priority groups. This scenario would result in a ~50% increase in the global PDR in the long-term reaching ~1.4 billion doses per year.

FIGURE 3: GLOBAL DEMAND FORECAST SCENARIOS, 2023-2034



The delivery of seasonal influenza vaccines to the WHO priority groups, all of which are outside of the infant immunisation schedule, is a significant challenge for many countries. The establishment and/or strengthening of sustainable approaches to vaccinate adult populations is critical to support more countries implementing seasonal influenza vaccination following WHO recommendations. Combined vaccines for multiple respiratory pathogens also have the potential to support increased seasonal influenza vaccine use through simplified programmatic requirements and reduced delivery costs. Programmatic suitability of available vaccines in low resource settings and the extent to which seasonal influenza vaccines are locally registered may also influence future adoption decisions. Ensuring availability of local influenza epidemiological data and financing amidst competing priorities will be necessary for the establishments and/or expansion of seasonal influenza vaccination programmes.

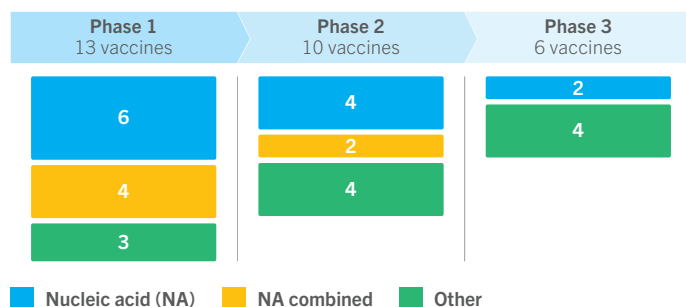
### Global Supply (Available Supply for Commercialisation)

Consultations with manufacturers and experts, as well as a review of publicly available information on seasonal influenza vaccines, provided the basis for an assessment of the current and future global available supply for commercialisation (ASC) of seasonal influenza vaccines.

As of November 2023, 29 seasonal influenza vaccines are in clinical development, 27 of which could be considered improved vaccines (Figure 4). Twenty of these vaccines are based on nucleic-acid (NA) technologies, either as stand-alone influenza vaccines (12) or as combination vaccines with influenza combined with other respiratory pathogens (8). Adjuvanted vaccines (1), high-dose vaccines (1), vaccines with innovative delivery systems (2) and recombinant vaccines (3) represent the improved vaccines in the pipeline. Vaccines considered to be universal and broadly protective against influenza viruses have been excluded based on the low probability of their availability in the market during the timeframe covered in this study.

Of the 29 seasonal influenza vaccines in the pipeline, 21 vaccines are being developed by nine new producers, creating a high likelihood of increasing supply to the market. Two of them are responsible for the development of 12 pipeline vaccines. The remaining eight pipeline vaccines are being developed by four producers of existing seasonal influenza vaccines. Newly developed vaccines by existing seasonal influenza vaccine producers will potentially replace currently produced vaccines and therefore not likely to increase the ASC.

FIGURE 4: SEASONAL INFLUENZA VACCINE PIPELINE BY CLINICAL DEVELOPMENT PHASE AND VACCINE TYPE



Nucleic acid-based vaccines comprise 69% of the influenza vaccines in clinical development. One of the potential benefits of nucleic acid-based vaccines is their ability to be manufactured relatively quickly, opening the potential for a reduced time lag between strain selection and vaccination and therefore, theoretically, improving their effectiveness by improving the match of circulating influenza strains and those contained in the vaccines. The global systems for strain selection would need revision to enable this potential benefit.

As of 2023, ASC is 1.2 billion trivalent-equivalent<sup>15</sup> doses. A base scenario modelling a modest increase of ASC from current producers and a typically paced entry of pipeline vaccines results in a 1.8-fold increase of ASC in the long-term compared to current ASC. To evaluate a range of future supply situations, scenarios were developed to model the impact of market exits, increases in production from existing manufacturers, and pipeline products reaching the market at different paces.

- A **low scenario** modelling limited market exits, minimal increase of ASC from current producers, and limited success in pipeline vaccine availability results in a 1.6-fold reduction of ASC in the short-term.

- A **high scenario** which modelled no market exits, modest increase of ASC from current producers, and an optimistic view of the progress of clinical development of pipeline vaccines would result in a 3-fold increase in ASC in the long term. Acceleration in the availability of NA vaccines may lead to ASC increases of up to 4-fold in the long-term. All sizeable increases of medium and long-term ASC would only materialise as a response to significantly increased demand, therefore careful coordination and planning is required.
- A **very low scenario** which is a worst case with low likelihood of occurrence, and which assumes that several current producers exit the market, was also modelled and would result in a 2-fold reduction in ASC in the short term; in the long-term, without increases in ASC from remaining producers in the market, or new market entrants, ASC would remain lower than current ASC in the base scenario.

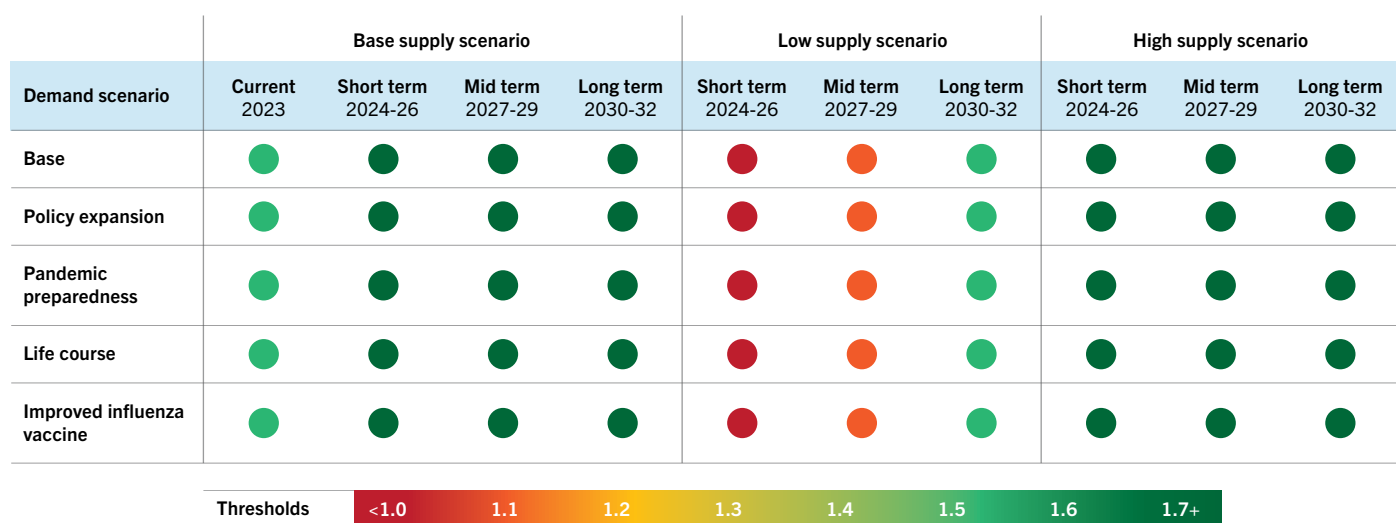
For manufacturers that supply to both hemispheres and produce both TIV and QIV vaccines, their ASC can be adjusted, to some degree, annually with respect to the proportions of TIV or QIV and northern or southern hemisphere vaccine doses that are made available.

### Supply / Demand Balance

For seasonal influenza vaccine, the current ASC in the base scenario is sufficient and exceeds demand by a margin that does not signal a risk of an imbalance between supply and demand. In the medium and long-term, ASC is likely to continue exceeding global demand in all scenarios. (Figure 5). Except for the low scenario, ASC is expected to exceed PDR. Due to the potential for pandemic influenza, excess ASC in seasonal influenza can be a benefit for pandemic preparedness. While ASC may exceed PDR, if significant demand from LIC and LMIC develops, access for them would need to be facilitated by manufacturers registering vaccines in those countries, providing vaccine that is programmatically suitable, and at sustainable prices.

The extent to which the estimated ASC is fungible and available to countries not currently using vaccine and for immediate access in advance of influenza transmission seasons (i.e., locally registered, available for immediate order) is not well understood.

FIGURE 5: SUPPLY/DEMAND BALANCE FOR BASE, LOW AND HIGH SUPPLY SCENARIOS



15 All ASC has been standardized to trivalent-equivalent doses to enable a dose-to-dose comparison and because manufacturing capacity is shared between quadrivalent and trivalent doses. It is assumed that each quadrivalent dose is equivalent to 1.25 trivalent doses.



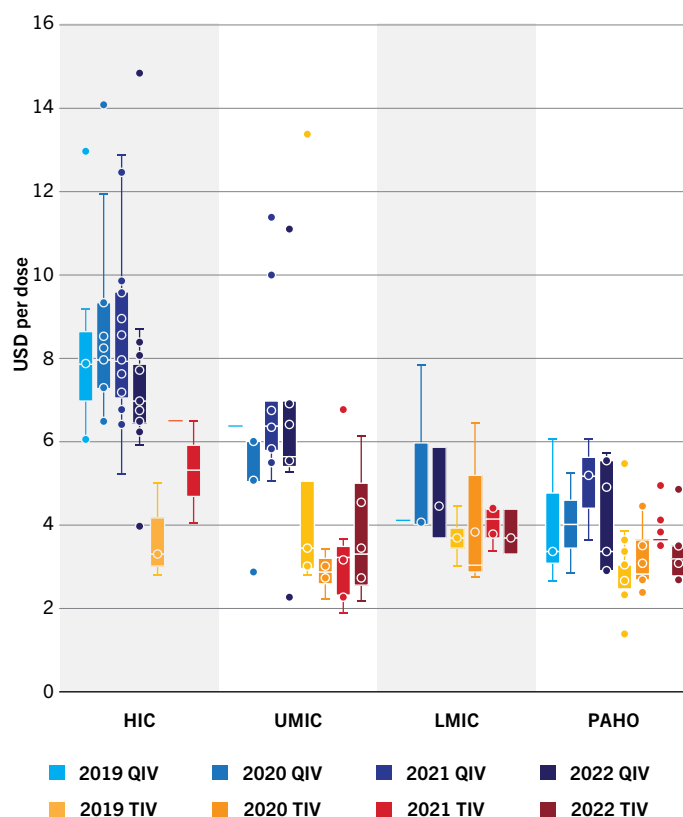
## Price

Prices reported by countries for seasonal influenza vaccines have been stable over time, with no discernible price trends within each type of vaccine or procurement method (Figure 6). When examining the adult formulations of QIV and TIV vaccines, they comprise more than 80% of global volume<sup>16</sup>, and tiering of prices across income groups is also evident, with an 8-fold and 10-fold difference in the highest and lowest reported median prices of adult formulation QIV and TIV prices between income groups, respectively. Median prices for adult QIV are consistently higher than those for adult TIV prices in all income groups with a narrower difference for the Pan American Health Organization Revolving Fund<sup>17</sup> (PAHO RF), the largest pool procurer of influenza vaccine. Tiered pricing can help support broader access and uptake of seasonal influenza vaccines in low resource settings.

Volumes do not appear to have an influence on price as there is no identifiable relationship between price and volume of adult QIV procured in HICs and LMICs and a weak downward price trend with higher volume in UMICs when viewed over the 2019-2022 timeframe (data not shown). Examination of the same data for adult trivalent seasonal influenza vaccine revealed a similar pattern (data not shown). This finding suggests that the market does not function according to conventional economic dynamics of supply and demand.

Pricing of improved seasonal influenza vaccines was reported by few countries and no conclusions can be drawn from the limited available data at the time of analysis.

FIGURE 6: PRICES OF ADULT QIV AND TIV DURING 2019 - 2022 AND BY INCOME GROUP



<sup>16</sup> MI4A dataset

<sup>17</sup> In Figure 5 countries that procure through the PAHO RF are included only in that grouping and have been removed from the other income-groups.

## Areas for Action

To maintain and increase timely and affordable access to seasonal influenza vaccines WHO will enhance alignment of partners and stakeholders to ensure coordination within a complex epidemiology, policy, regulatory, access and delivery ecosystem. Specifically, WHO will focus in three areas:

### Country demand, policy, and uptake

- WHO to support Member States to improve the monitoring of influenza vaccination coverage among targeted groups and the general population, document lessons learned from successful influenza vaccination initiatives (e.g. PAHO), to support coverage improvements and guide Member States to assess the full value of influenza relative to other vaccines and inform strategic trade-off decisions on influenza vaccine policy and use.

### Enabling environment for access to current vaccines

- WHO to heighten coordination across stakeholders for successful transition from QIV to TIV, including monitoring and promoting active communication regarding the evolution of Member State formulation needs, and the evolution of vaccine supply and demand.
- WHO to enhance transparent communication with industry, regulatory agencies, and partners on the process for future vaccine formulation recommendations.
- WHO and partners to evaluate country product preferences and willingness-to-pay for current influenza vaccines, including impact of regional manufacturing efforts, to understand likelihood of future adoption and potential supply needs.

### Enabling environment for pipeline vaccines

- WHO to actively monitor the clinical development pipeline to assess the progress and likelihood of success that new vaccines will reach the market and create a conducive environment:
  - Developing policy recommendations and guidance to inform country product selection (amid increasing choice).
  - Planning for potential changes to processes and timelines for semi-annual strain selection (i.e., for new vaccines with faster manufacturing process, strain selection could occur closer to influenza vaccination).

## Methodology and Sources

**Market Access for Vaccines Technical Advisory Group MI4A** benefits from the expertise of a standing advisory group for input, review and validation of market analyses:

<https://www.who.int/teams/immunization-vaccines-and-biologicals/vaccine-access/mi4a/technical-advisory-group-mi4a>

**Demand:** Historical procurement data (2023 WHO MI4A dataset and consultation with experts)

**Supply:** Manufacturer consultations, 2023 WHO MI4A dataset, publicly available information, and media reports.

**Pricing:** Historical data review (MI4A Vaccine Purchase Database, UNICEF SD, PAHO RF)

### Other Useful Public Resources

**WHO position paper on vaccines against influenza** – May 2022. Geneva: World Health Organization; 2022 (<https://www.who.int/publications/i/item/who-wer9719> accessed 11 October 2023)

**WHO Global Influenza Strategy 2019-2030** ([Global Influenza Strategy 2019–2030 \(who.int\)](https://www.who.int/publications/i/item/9789241512466-eng))

**WHO Preferred Product Characteristics for improved influenza vaccines** ([9789241512466-eng.pdf \(who.int\)](https://www.who.int/publications/i/item/9789241512466-eng))

**WHO/UNICEF Joint Reporting Form on influenza vaccination policy** ([Influenza vaccination policy \(who.int\)](https://www.who.int/publications/i/item/9789241512466-eng)) and on influenza vaccine coverage ([Influenza vaccination coverage \(who.int\)](https://www.who.int/publications/i/item/9789241512466-eng))

**UNICEF Seasonal Influenza Vaccine Supply Update** ([Seasonal-influenza-vaccine-supply-note-September-2020.pdf \(unicef.org\)](https://www.unicef.org/publications/seasonal-influenza-vaccine-supply-note-september-2020))

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