OLIVER WYMAN

Health & Life Sciences



March 2009

# Influenza Vaccine Supply and Demand

## Summary of Findings

## May 2009

# Important update related to the current outbreak of H1N1 “swine flu”

The following study by Oliver Wyman evaluated the production capacity for seasonal influenza vaccine as well as production timelines and capacity for **H5N1 (avian) influenza vaccine**. It was released in early 2009 in conjunction with a broader analysis of the logistics, cost, and possible financing options for establishing an international stockpile of an H5N1 vaccine. That broader analysis was conducted by Oliver Wyman in collaboration with the World Health Organization (WHO) and the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA).

The study should not be used to make any prediction about the timelines and production capacity for a vaccine against the new **A/H1N1 “swine flu” strain**. This outbreak is still in early days, and there are significant differences between the H5N1 and the new H1N1 strains. Thus, there are uncertainties that will impact the timelines and production capacity of a vaccine against this new strain. For instance, open questions remain around the required dosage levels and production yields for the new strain.

While this study is not yet applicable to the current situation, it has helped lay the foundation for a quick assessment of vaccine timelines and production capacity for H1N1. The study collaborators are working to resolve the uncertainties and will then utilize the models generated during the study to produce new estimates. Please contact Oliver Wyman for questions related to the initial study, and contact the WHO and the IFPMA around recent developments related to H1N1.

# Executive summary (1 of 2)—From Press Release on February 24, 2009

Vaccine manufacturers have substantially increased their capacity to produce pandemic influenza vaccines during the past two years, according to a new study by Oliver Wyman, an international strategy consulting firm. Importantly, this study arrived at capacity estimate numbers that the global health community agrees upon, after considerable prior debate.

Conducted in collaboration with the World Health Organization (WHO) and The International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)[1], the new study finds that while capacity is increasing, it would not be sufficient to meet the global need for emergency production of pandemic influenza vaccines at the time of a pandemic. However, the study notes that current and future surplus capacity could support the production of billions of doses of H5N1 influenza vaccine prior to a pandemic for stockpiling efforts and other utilization.

"We found that considerable progress has been made to enhance the production capacity of pandemic influenza vaccine," said Adam Sabow, partner at Oliver Wyman who led the study. "While capacity still falls short of global need during a pandemic, the surplus capacity during the inter-pandemic period creates opportunities for preparedness efforts. For example, we are working with the WHO to design a global H5N1 vaccine stockpile. If demand does not exist to utilize this excess capacity, however, manufacturers are likely to rationalize some of it, creating further shortages at the time of a pandemic."

IFPMA Director General Alicia D. Greenidge said, "This study advances our understanding of the world's ability to address pandemic influenza, and demonstrates the progress made by our member companies in developing new vaccine technologies and expanding production facilities. Our member companies are committed to working with the WHO and countries to ensure that we make the best use of the surplus capacity to prepare for a pandemic. The findings suggest that the early use of stockpiled H5N1-based vaccines, followed by pandemic vaccines as soon as these become available, offers a realistic strategy to address this significant threat."

1 Oliver Wyman also consulted with 11 other current or potential influenza vaccine manufacturers in developing countries which are not members of the IFPMA.

# Executive summary (2 of 2)—From Press Release on February 24, 2009

The new Oliver Wyman study provides a number of further insights:

- Pandemic influenza vaccine production capacity has increased by 300 percent over the last two years, largely driven by improvements in production yields and dosage-sparing technologies.
- With current technology, doses of vaccine tailored to the actual pandemic influenza strain will not be available until four months after identification of that strain by the WHO due to the technical lead time required to adapt the strain for vaccine production, manufacture vaccine, and distribute product.
- In the base (most likely) case[2], manufacturers could produce 2.5 billion doses of pandemic vaccine in the 12 months following receipt of the production strain, requiring 4 years to satisfy global demand. In the best case, 7.7 billion doses could be produced in the first 12 months, requiring 1 ½ years to satisfy global demand.
- This capacity is expected to rise to 5 - 14.5 billion doses over the next five years. The resulting time to meet global demand would be reduced to between 2½ years (in the base case) and 1 year (in the best case).
- Surplus capacity (above current seasonal influenza and stockpile demand) currently exists to produce 2.5 billion annual doses of H5N1 vaccine prior to a pandemic. This surplus capacity is expected to rise to between 2.6 and 5.4 billion doses per year over the next 5 years.

Oliver Wyman initiated this study in 2008 in cooperation with the WHO and the IFPMA, with funding from the Bill & Melinda Gates Foundation.

2 The “base” and “best” cases are based on different assumptions relating to a number of factors, including the level of demand for seasonal influenza and H5N1 vaccine in the inter-pandemic period, the yields that can be attained, the level of antigen-sparing achievable and the degree of rationalization of traditional egg-based vaccine production capacity as new cell-based capacity comes on line. In both cases, effective coverage is calculated based on 2 doses per person, for a global population of 6.7 billion.

# Project background

## Why was it important to update the supply/demand map?

### Supply

- Facility plans have progressed
  - New facilities and existing facility expansions have been announced
  - Many new projects are planned in the developing world
- Antigen per dose requirements are lower
  - Additional manufacturers are now using antigen-sparing adjuvants
  - Standard alum-adjuvanted H5N1 dosage has decreased from 30 ug to 15 ug
- Yields have improved
  - Vietnam strain, with yields 1/3 of seasonal, was unusually low-yielding
  - Indonesia strain has yields that are equal to or better than seasonal

### Demand

- Stockpiling demand was not quantified in the original work
  - Major stockpile holders' current stockpiles and replenishment plans are now included
- Additional seasonal demand data is now available
  - More recent and comprehensive coverage data is available from the Macroepidemiology of Influenza Vaccination (MIV) Study Group

Source: Macroepidemiology of Influenza Vaccination (MIV) Study Group. Corresponding author: David S. Fedson, MD 57, chemin du Lavoir / 01630 Sergy Haut, France.

## Capacity estimation sources

This analysis was informed by interviews with manufacturers, stockpile holders, and industry experts as well as an iterative review process with IFPMA.

### Seasonal influenza vaccine capacity

- Interviews with 17 present and emerging manufacturers, including IIV and LAIV production
- Interviews with additional experts and organizations, including WHO, IFPMA, and DCVMN
- Supplemented with secondary research
- Modeling of 44 present and planned facilities in 24 countries

### Pandemic (H5N1) vaccine conversion assumptions

- Interviews with present H5N1 vaccine manufacturers to understand their dosages and yields
- Review of trial data for relevant H5N1 vaccines

### Seasonal influenza vaccine demand

- Individual country demand data from the MIV Study Group[1] – accounts for >95% of doses distributed worldwide in 2005
- Supplemented with secondary research for 2006 and 2007 demand in key countries

### H5N1 vaccine stockpile demand

- Interviews and / or site visits with major H5N1 vaccine stockpile holders
- Interviews with manufacturers who have provided H5N1 vaccine for stockpiles
- Supplemented with secondary research

1 Macroepidemiology of Influenza Vaccination (MIV) Study Group. Corresponding author: David S. Fedson, MD 57, chemin du Lavoir / 01630 Sergy Haut, France.

# Seasonal influenza vaccine capacity projection

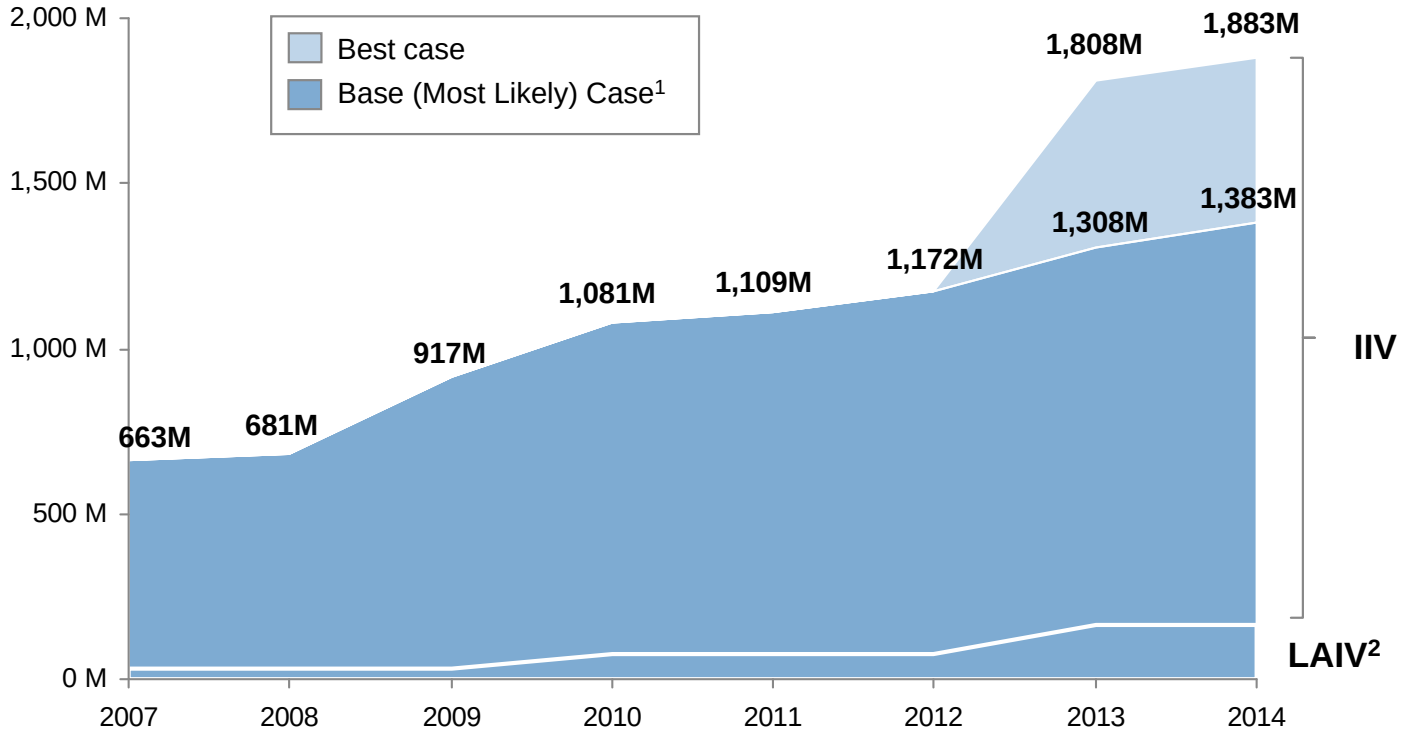
Influenza vaccine capacity is expected to more than double by 2014 in the base (most likely) case.

## Assumptions

- Base (most likely) case assumes that when the US sponsored cell facilities come on-line, the same amount of egg-based capacity will be rationalized
- The best case assumes that there will be no rationalization of capacity when the US cell facilities come on-line

**Influence vaccine capacity**

Seasonal influenza vaccine doses per year, assuming 10 months of operation




1 Developing world capacity represents 13% of most likely capacity in 2009, rising to ~20% in 2014 (probability weighted).
2 LAIV accounts for fill constraints at manufacturers
Note: Recombinant approaches not included; focus was on technologies with existing licensed influenza products.

# Pandemic influenza vaccine capacity at the point of a pandemic—Assumptions

We have established a common set of assumptions for the conversion from seasonal to pandemic vaccine capacity.

| | Base (Most Likely) Case | Best Case |
|---|---|---|
| **Scenario Definition** | ▪ Case believed to be most likely based on current understanding of production | ▪ Reasonable best case to provide a realistic best case of potential capacity |
| **Capacity Included** | ▪ Egg-based capacity is rationalized when US cell facilities come on-line (equal to cell-based expansion)<br>▪ LAIV excluded given lack of pandemic licensure | ▪ No rationalization of egg-based facilities<br>▪ LAIV included – pandemic vaccine volumes limited by filling[2] |
| **Dosage** | ▪ Assumes that manufactures will only be able to use antigen-sparing technology when their vaccines have been licensed at that dosage[1]<br>– Alum adjuvanted = 15ug / dose<br>– Novel adjuvanted = 3.8 – 7.5ug / dose<br>– Wild type = 3.8 – 7.5ug / dose | ▪ Assumes that manufactures will be allowed to produce at dosages corresponding to their most recent successful trials[1]<br>– Results in additional manufacturers at lower end of dosage ranges |
| **Yield** | ▪ 1:2 yields for pandemic: seasonal<br>– To reflect risk of low-yielding strain | ▪ 1:1 yields for pandemic: seasonal<br>– Assumes high-yielding strain |
| **Facility "push" factor** | ▪ 10% increase in capacity during the pandemic period | ▪ 10% increase in capacity during the pandemic period |
| **Timing (from mfg. receipt of prod. strain)** | ▪ First cell doses in 10 - 12 weeks<br>▪ First egg doses in 12 weeks | ▪ First cell doses in 10 - 12 weeks<br>▪ First egg doses in 12 weeks |

1 Antigen per dose in ranges from 9.2ug in 2009 to 5.4 in 2014 in the most likely case and 5.0 in 2009 to 5.5 in 2014 in the best case.
2 LAIV pandemic capacity constrained by filling capacity at manufacturers; recombinant excluded

# Pandemic influenza vaccine capacity at the point of a pandemic

Real-time pandemic vaccine capacity will fall short of need, taking over 1 year to satisfy global demand even in the 2014 best case.

**Pandemic doses produced (cumulative)**

| Production window (# of months post receipt of reference strain by manufacturers to complete production[1]) | *2009* Base (Most Likely) Case | *2009* Best Case[2] | *2014* Base (Most Likely) Case | *2014* Best Case[2] |
|---|---|---|---|---|
| 3 | 65M | 190M | 130M | 380M |
| 4 | 340M | 1,060M | 700M | 2,040M |
| 5 | 580M | 1,820M | 1,220M | 3,500M |
| 6 | 860M | 2,680M | 1,790M | 5,140M |
| 12 | 2,450M | 7,660M | 5,120M | 14,690M |
| **Time to meet global demand:** | **49 months** (4.1 years) | **20 months** (1.7 years) | **28 months** (2.4 years) | **12 months** (1.0 years) |

1 To this timing should be added 3 - 4 weeks from time of pandemic declaration to create reference strain – remaining two weeks of pathogenicity testing will occur after strain release

2 LAIV included in best case represents ~10M doses per month (~1% of total pandemic capacity) in 2009 and ~20M doses per month (~1% of total pandemic capacity) in 2014

Note: Recombinant excluded. Source: Oliver Wyman analysis.

# Inter-pandemic H5N1 vaccine surplus capacity estimation methodology

We have also estimated inactivated vaccine surplus capacity available in the inter-pandemic period.

**Seasonal influenza vaccine capacity** - **Seasonal influenza vaccine demand** - **H5N1 vaccine stockpile demand** = **Surplus seasonal influenza vaccine capacity**

1. Compile current production data and manufacturer-stated capacity[1]
2. Convert to total capacity for ten months of production
3. Project future capacity expansions (weighted by likelihood of construction) and rationalizations

1. Model current demand from seasonal influenza immunization programs
2. Project future seasonal demand growth (high and low surplus capacity scenarios)

1. Model current H5N1 vaccine stockpile demand
2. Expectation of country stockpile replenishment and new stockpile acquisition (for existing stockpile holders and likely new country stockpiles)

---

**Surplus seasonal influenza vaccine capacity** x **H5N1 vaccine conversion assumptions** = **Surplus H5N1 vaccine capacity available**

1. Convert seasonal influenza vaccine to H5N1 vaccine yields
2. Model H5N1 vaccine dosages

1 LAIV and recombinant excluded because H5N1 vaccine products have not been submitted for approval

# Inter-pandemic capacity estimates—Demand assumptions

The inter-pandemic influenza vaccine demand assumptions were based on historical seasonal vaccine and projected H5N1 vaccine stockpile demand.

| | High Surplus Capacity Case | Low Surplus Capacity Case |
|---|---|---|
| **Scenario Definition:** | ▪ Case that provides a realistic upper limit to available capacity for H5N1 vaccine production in the inter-pandemic period | ▪ Case that provides a realistic lower limit to available capacity for H5N1 vaccine production in the inter-pandemic period |
| **Seasonal Influenza Vaccine Demand:** | ▪ Demand modeled for individual countries<br>– Plotted best fit curves and derived equations from regressions of historical data<br>▪ Regressions recalculated with updated data<br>– New MIV study group[1] data added for 17 new countries<br>– Updated MIV data added for 55 countries<br>– Secondary research provided 2006 and 2007 data for key countries | ▪ Based on continued historic growth, estimated at 10.3% per year from 1997 - 2006<br>– Increased coverage and new sub-populations for established programs<br>– Additional countries adopting programs beyond high surplus capacity case |
| **H5N1 Vaccine Stockpile Demand:** | ▪ Existing stockpile holders continue to stockpile at current rates with current form of vaccine<br>▪ Stockpiles replenished based on best estimates<br>– Every 3 years for filled doses<br>– Every 5 years for bulk vaccine<br>▪ Assume 1:1 H5N1 to seasonal yields | ▪ Existing stockpile holders and highest likelihood new country stockpilers build H5N1 vaccine stockpiles for 50% of their populations<br>– Accounting for 1B doses<br>▪ All stockpile holders hold filled doses that must be replenished every 2 years<br>▪ Assume 1:1 H5N1 to seasonal yields |

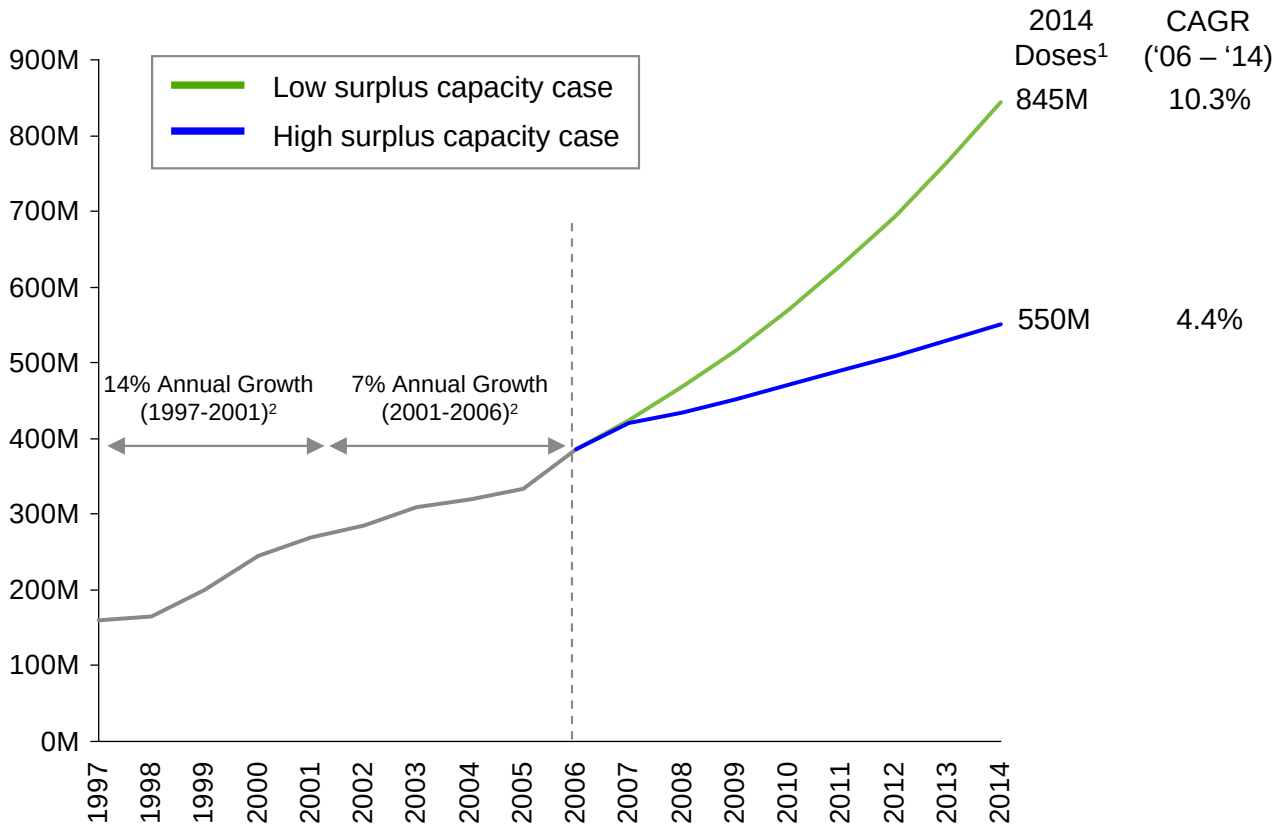
1 Macroepidemiology of Influenza Vaccination (MIV) Study Group. Corresponding author: David S. Fedson, MD 57, chemin du Lavoir / 01630 Sergy Haut, France.

# Inter-pandemic capacity estimates—Seasonal demand

Seasonal influenza vaccine demand is projected to grow at 4 – 10% per year.

**Estimated seasonal influenza vaccine demand**

Seasonal doses per year




## Implications

- If demand grows as projected based on individual country analysis, it will decline relative to its historic rates
- If demand continues to grow at historical rates, the CAGR will exceed even a universal coverage recommendation scenario (with reasonable assumptions)

Source: Healthy People 2010 website; MIV Study Group Reports (2005 and 2007); UNPD Population Data Set; CDC report "Estimates of Influenza Vaccination Target Population Sizes in 2006 and Recent Vaccine Uptake Levels"; expert interviews; Oliver Wyman analysis.

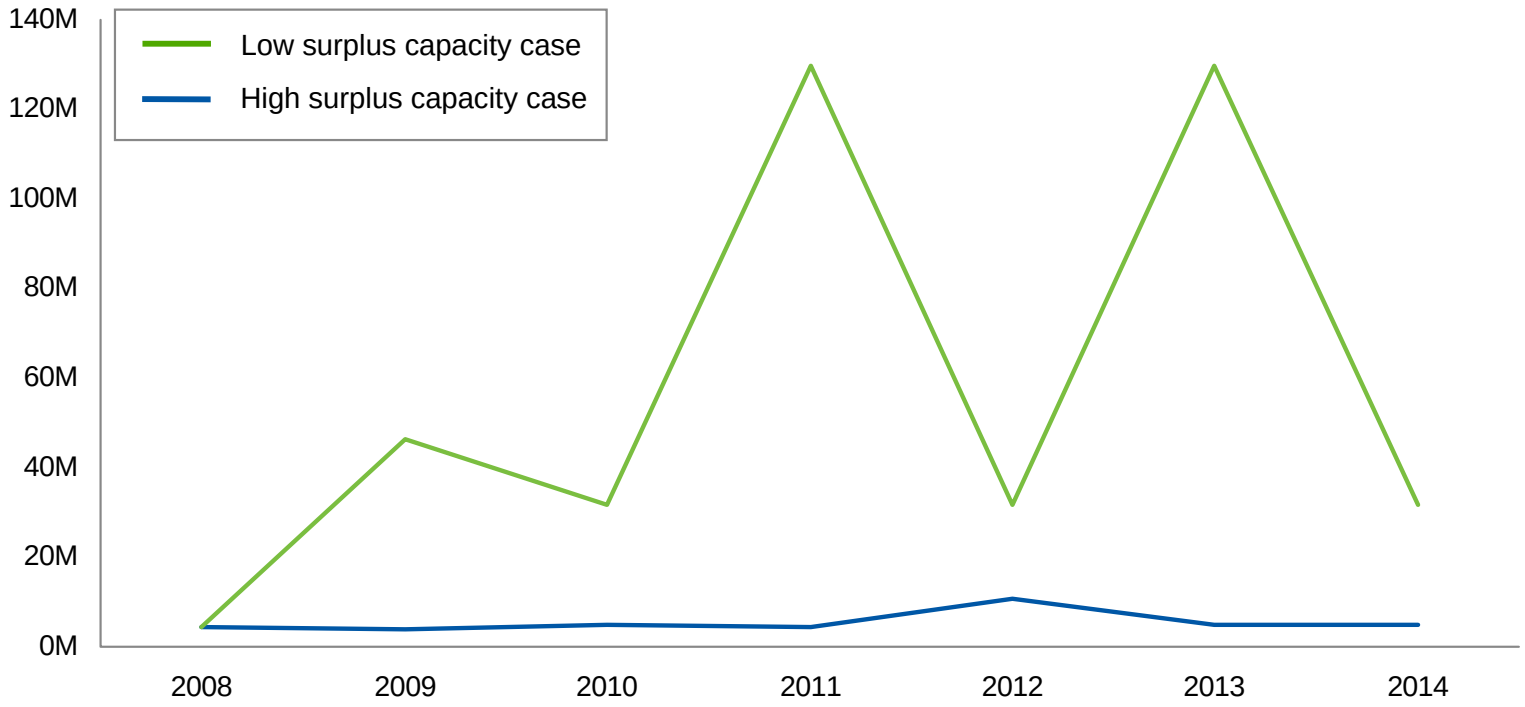
Note: No data available for 2004, given unexpected vaccine supply interruption. Figure shown is an interpolated estimate.

# Inter-pandemic capacity estimates—Stockpile demand

Even in the low surplus capacity scenario, demand from existing and highest likelihood country stockpiles will be a minor draw on capacity, averaging less than 5% of capacity.

**Estimated future stockpile demand (2008 – 2014)**

Equivalent seasonal doses[1]




| | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 |
|---|---|---|---|---|---|---|---|
| "Low surplus capacity" case % of capacity: | 0.7% | 5.2% | 3.2% | 12.6% | 2.9% | 7.9% | 1.9% |
| "High surplus capacity" case % of capacity: | 0.7% | 0.5% | 0.5% | 0.4% | 1.0% | 0.3% | 0.3% |

Source: Expert interviews, Oliver Wyman analysis.

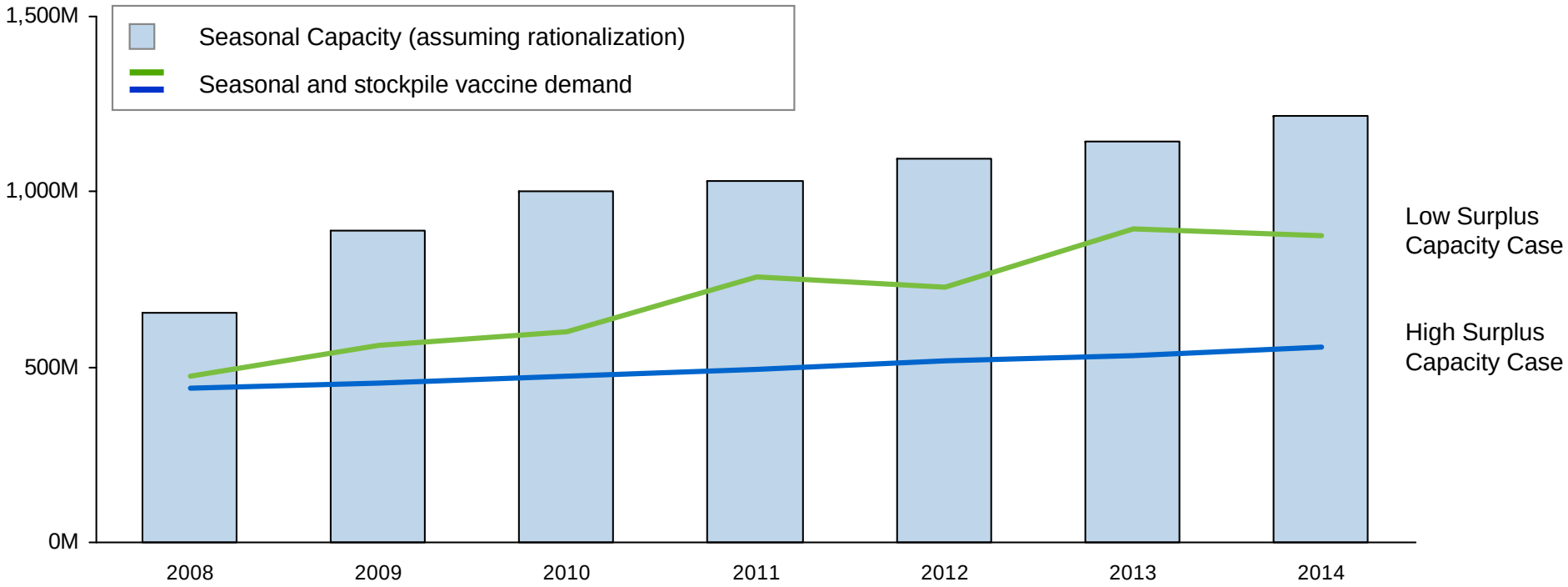
1 Assumes 1:1 seasonal and H5N1 yields; antigen converted from H5N1 doses to 45 ug seasonal doses.

# Inter-pandemic capacity estimates—Surplus seasonal influenza vaccine capacity

Even if some egg-based capacity is assumed to be rationalization, considerable surplus capacity remains for inter-pandemic production.

**Influenza vaccine capacity vs. demand**

Represented in seasonal-equivalent doses




| **Surplus Capacity** (Doses[2]): | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 |
|---|---|---|---|---|---|---|---|
| Low Surplus Capacity: | 179M | 325M | 401M | 272M | 368M | 246M | 340M |
| High Surplus Capacity: | 214M | 432M | 528M | 537M | 574M | 608M | 662M |

Note: Excludes LAIV and recombinant capacity. Based on most likely capacity estimates, assumes that some egg-based capacity is rationalized when US sponsored cell facilities come on-line

Source: Healthy People 2010 website; MIV Study Group Reports (2005 and 2007); UNPD Population Data Set; CDC report "Estimates of Influenza Vaccination Target Population Sizes in 2006 and Recent Vaccine Uptake Levels"; company reports; expert interviews; Oliver Wyman analysis.

# Inter-pandemic capacity estimates – H5N1 conversion assumptions

A similar set of conversion assumptions were used as in the pandemic vaccine capacity estimates (and are consistent across the high and low surplus cases).

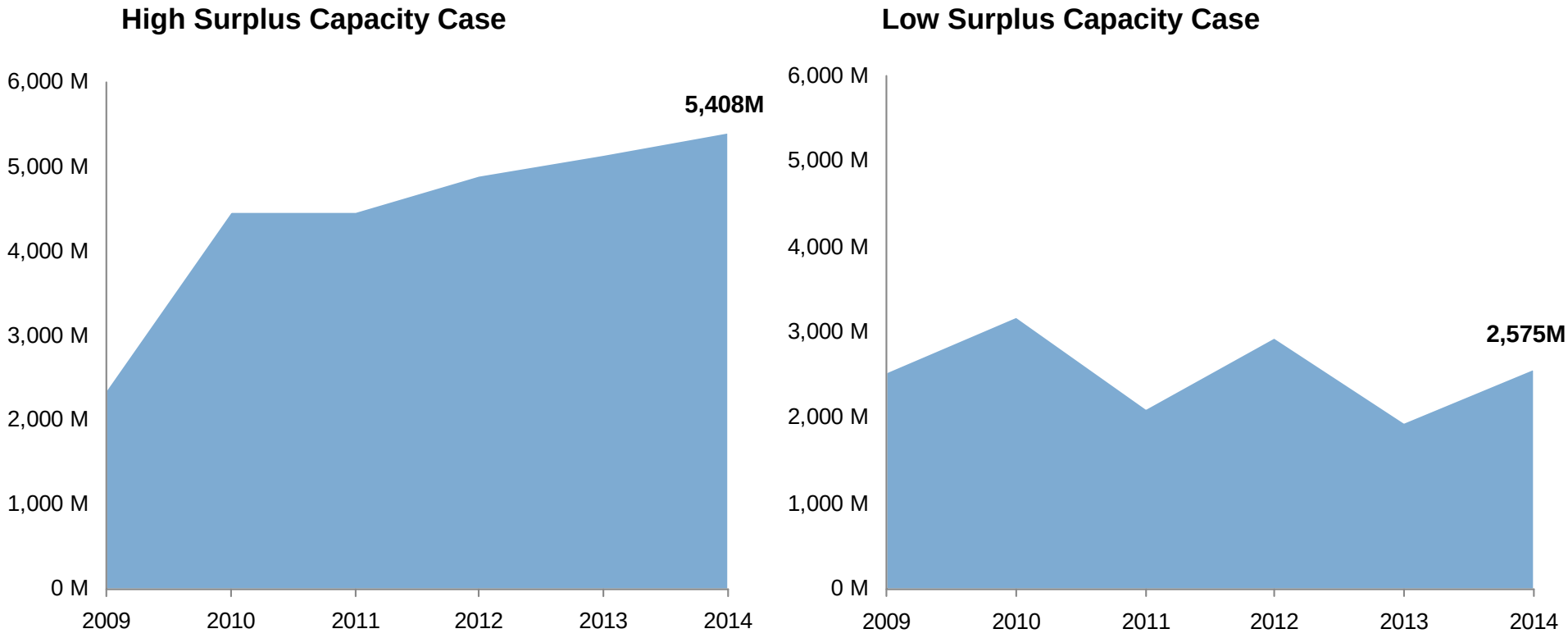
| | High Surplus Capacity Case | Low Surplus Capacity Case |
|---|---|---|
| **Scenario Definition** | ▪ Case that provides a realistic upper limit to available capacity for H5N1 vaccine production in the inter-pandemic period | ▪ Case that provides a realistic lower limit to available capacity for H5N1 vaccine production in the inter-pandemic period |
| **Capacity Included** | ▪ Base (most likely) Case - egg-based capacity is rationalized when US cell facilities come on-line<br>▪ LAIV excluded based on lack of viable H5N1 vaccine | ▪ Base (most likely) Case - egg-based capacity is rationalized when US cell facilities come on-line<br>▪ LAIV excluded based on lack of viable H5N1 vaccine |
| **Dosage** | ▪ Assumes that manufactures will only be able to use antigen sparing technology when their vaccines have been licensed at that dosage<br>– Alum adjuvanted = 15ug / dose<br>– Novel adjuvanted = 3.8 – 7.5ug / dose<br>– Wild type = 3.8 – 7.5ug / dose | ▪ Assumes that manufactures will only be able to use antigen sparing technology when their vaccines have been licensed at that dosage<br>– Alum adjuvanted = 30ug / dose<br>– Novel adjuvanted = 3.8 – 7.5ug / dose<br>– Wild type = 3.8 – 7.5ug / dose |
| **Yield** | ▪ 1:1 yields for H5N1: seasonal<br>– Based on assumptions that high-yielding strains will be used for production | ▪ 1:1 yields for H5N1: seasonal<br>– Based on assumptions that high-yielding strains will be used for production |

# Inter-pandemic capacity estimates—Surplus H5N1 vaccine capacity available

Even in the low surplus capacity case, over two billion doses of H5N1 vaccine could be produced in the inter-pandemic period and that amount will rise into the future.

## H5N1 vaccine capacity available[1]

Inactivated H5N1 doses available per year




Source: Oliver Wyman analysis.

1 Seasonal vaccine doses remaining after seasonal demand and stockpile needs are met, then converted into H5N1 vaccine doses. Does not include either LAIV or recombinant capacity.

# OLIVER WYMAN


MARSH MERCER KROLL
GUY CARPENTER OLIVER WYMAN