

Influenza Global Vaccine Supply

Current status of vaccine production and Pandemic preparedness

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When a pandemic threat appears

Current Situation

- Vaccine manufacturers will not be able to meet the demand
- Non-producing countries will not have vaccine

What can be done?

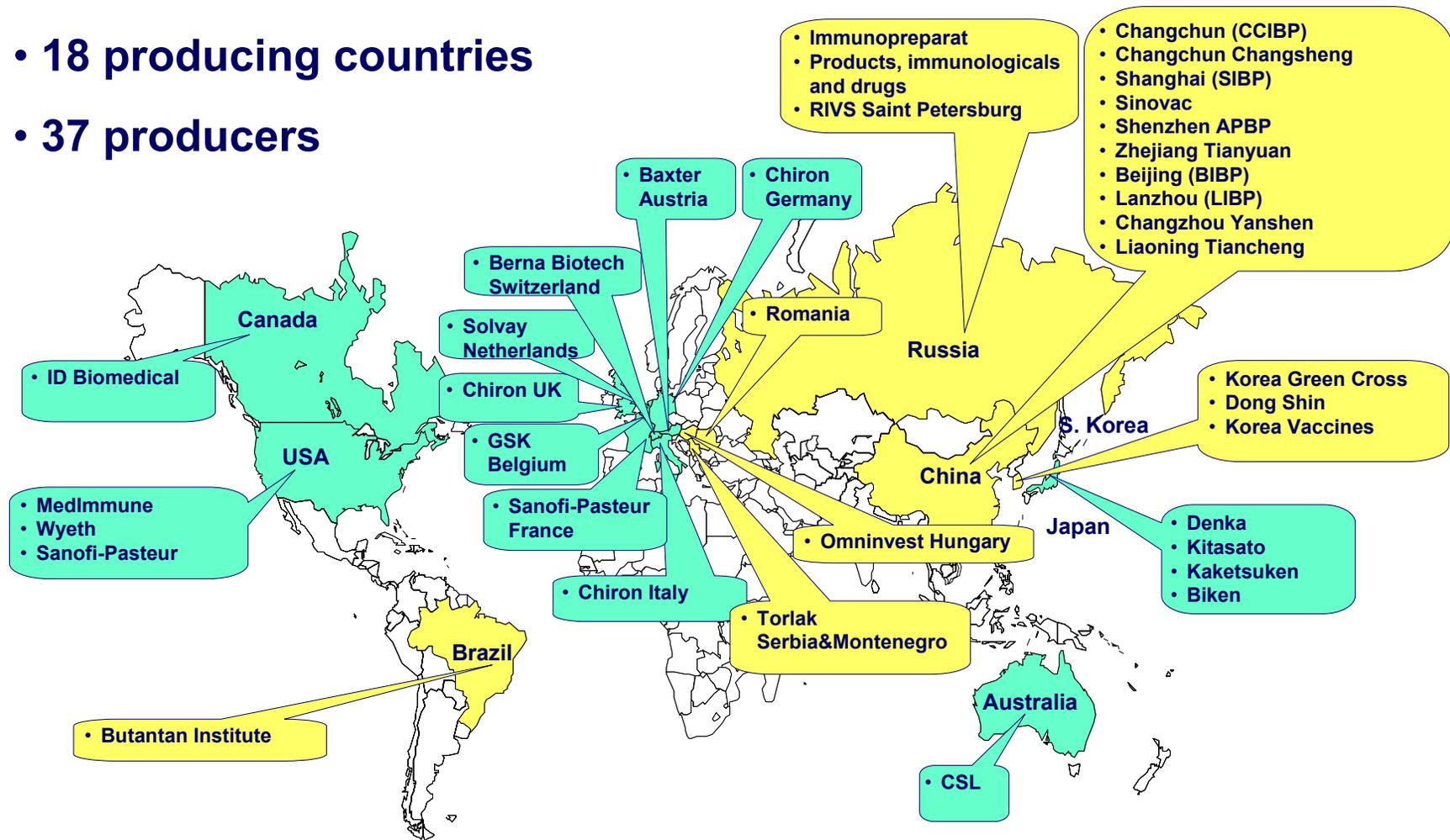
- Increase uptake of seasonal vaccine to increase production capacity
- With better knowledge of the forecast demand for seasonal vaccine, companies would be in a better position to produce pandemic vaccine

This does not solve the vaccine shortage now



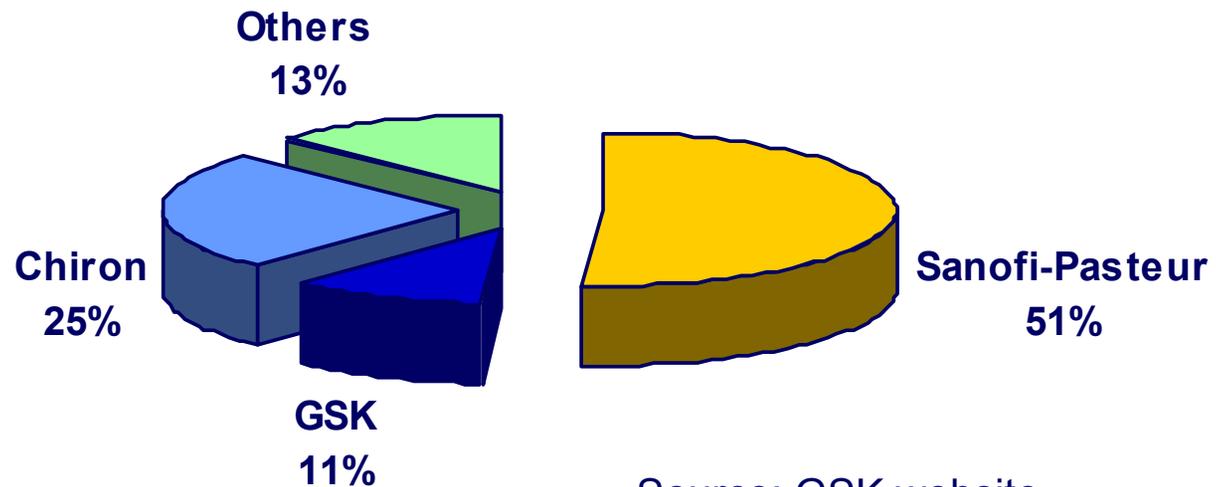
Current vaccine production capacity

- 18 producing countries
- 37 producers



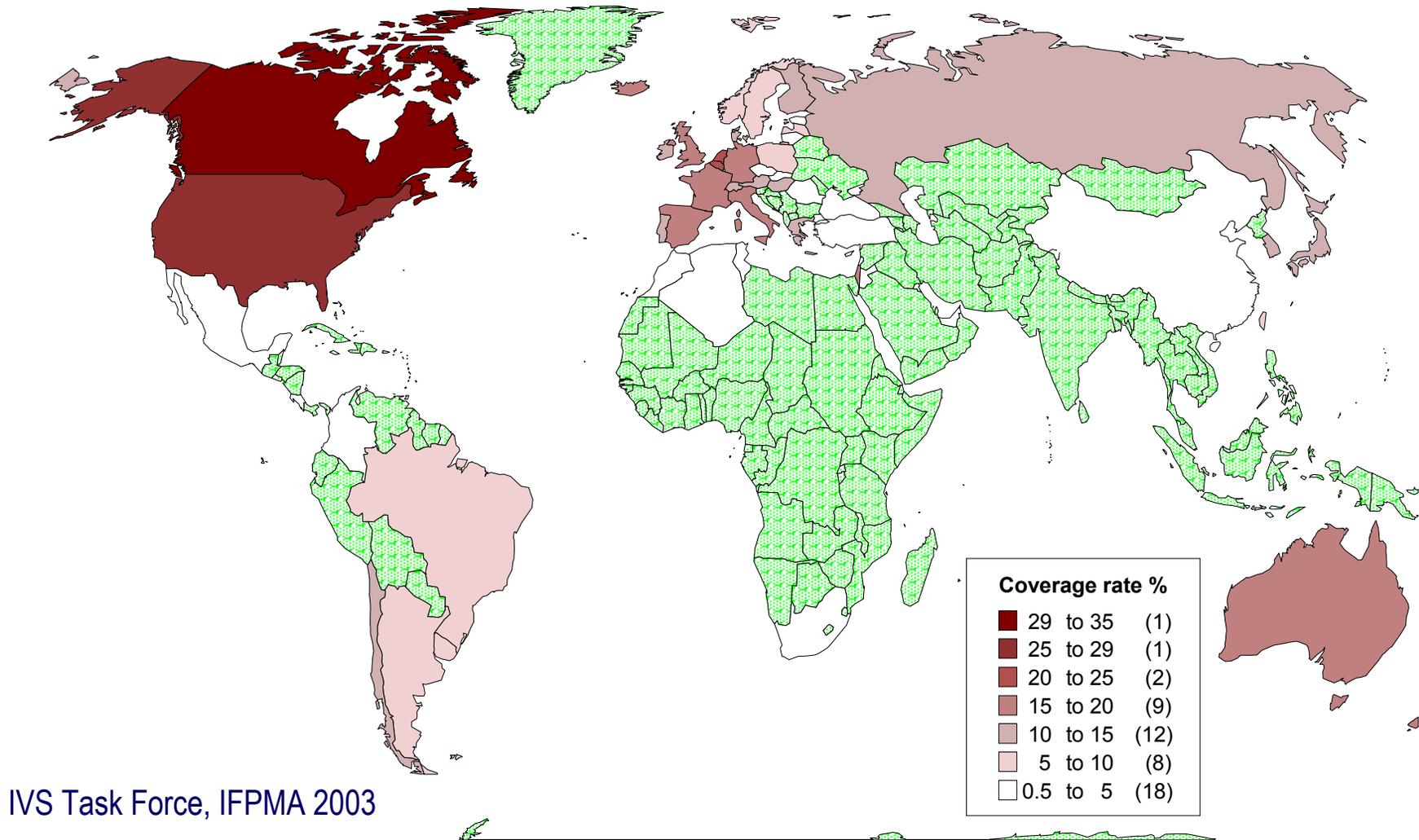
Current vaccine production capacity

- Maximum installed capacity = 420 Md + 30 Md fillers
- Current trivalent vaccine production = 350 Md
 - 300 Md produced for the global market (Europe, North America, Australia)
 - 50 Md for local use (China, Russia, Japan)



Source: GSK website

Influenza Vaccine Consumption



IVS Task Force, IFPMA 2003



Pandemic Influenza vaccine

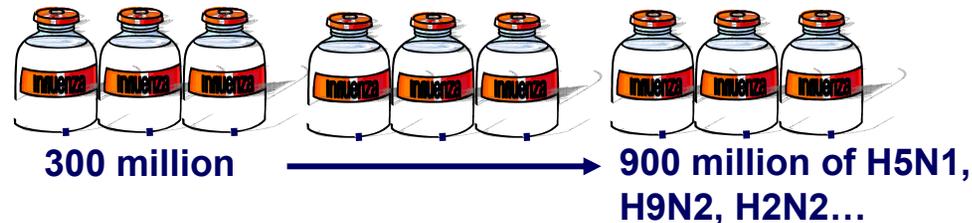
Options for increasing production capacity

1. Smart composition and/or formulation
2. New application forms
3. Increase use of seasonal vaccine in developed and developing countries
4. Continue dialogue with vaccine industry
 - Vaccine production is highly concentrated in Europe and North America



Increasing production capacity

1. Smart composition

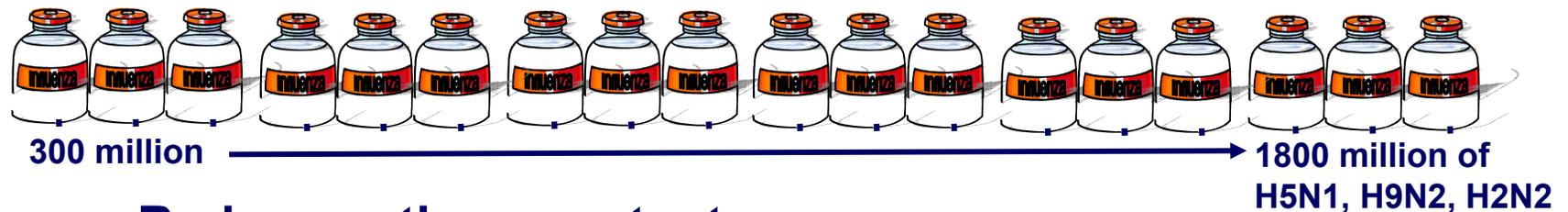


- All manufacturers working with reference virus developed by WHO (12 manufacturers from 11 countries)
 - Clinical trials being evaluated (H5N1, H9N2, H2N2,...)
 - There is a research agenda
 - Regulatory issues being considered
- Results H5 N1: safety and immunogenicity

Preliminary data suggest that H5N1 is safe, well tolerated and immunogenic

Increasing production capacity

1. Smart composition



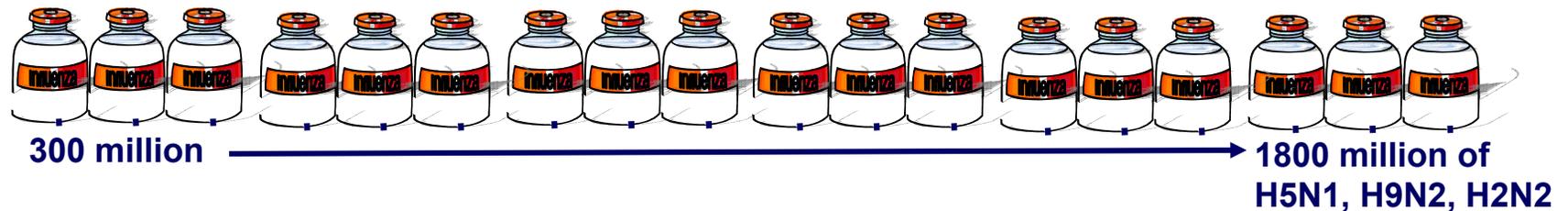
- **Reduce antigen content**
 - **Sparing: 50% works, but 2 dose schedule (first results Dec 2006)**
 - **Adjuvant: Alum increases vaccine immunogenicity.**
- **Regulatory requirements**
 - **Harmonization between EMEA, FDA and developing countries**

WHO meetings in 2006 to facilitate regulatory agreement among developed and developing countries



Increasing production capacity

2. New application forms

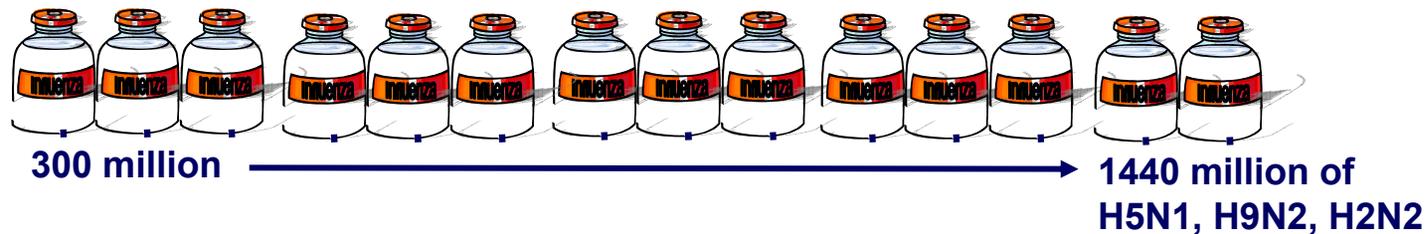


- Possible 7,5 μg per dose
 - Intradermal vaccination, need of more clinical data
 - Difficult to implement for mass vaccination campaigns

Considerable level of uncertainty

Increasing production capacity

3. Increase seasonal vaccine coverage in *developed countries* to 75%



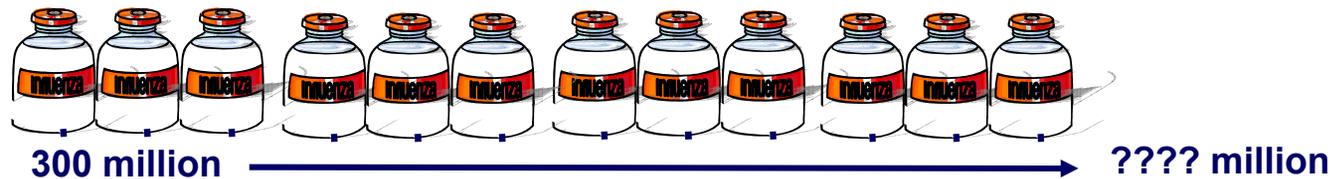
- Age over 50 in
- Those at highest risk
- WHO's target is increase coverage by 60% in 2010

The improved coverage will increase vaccine production by 60%



Increasing production capacity

3. Increase seasonal vaccine coverage in *developing countries*



- Assist countries on feasibility of local vaccine production (e.g. Thailand)
- Assist countries on regulatory issues, licensing, quality control, standardization (IVB/GIP)
- Assist countries on disease burden studies
- Support to technology transfer

Looking for solutions

4. Continued dialogue with the vaccine industry
 - Second meeting on Influenza vaccines that induce broad spectrum and long lasting immuno-responses, December 2005
 - WHO meeting in January 2006 with the veterinary vaccine manufacturers and regulators
 - Feasibility of using veterinary production facilities for pandemic
 - Regulatory constrains
 - WHO meeting in February 2006 with NRAs, scientific experts and vaccine manufacturers
 - Options to reduce vaccine supply gap in short, medium and long term for seasonal vaccine (cell culture, new facilities)
 - Options for a pandemic vaccine, H5N1, formulations, antigen content, adjuvants
 - Options for increasing vaccine production capacity during pandemic



Influenza pandemic

- Assuming: 900 million doses in 8 months = 3.75 million/day



- Early outbreak detection, diagnosis and notification is essential

The lead time to start production will depend on:

- access to the pandemic virus (7-21 days)
 - development of prototype i.e. NIBSC (21-51 days)
 - Registration (45-60 days), EMEA = 1day
- } 270 Md } 495 Md

Solutions?

- **Short and medium term**
 - R&D for antigen reduction, adjuvants, intradermal use, etc
 - Increase seasonal vaccine use ⇒ manufacturer will be better prepared for production of pandemic vaccines
 - Manufacturers' plans to expand capacity by 2008
 - Early start of vaccine production
- **Long term**
 - New vaccines: cell lines production, new formulations, new strains; cross and long lasting immunogenicity
- **Radical solution required (seasonal + pandemic vaccines)**



Influenza pandemic vaccines

- **Goals:**
 - in pandemic; equitable and timely supply
 - inter-pandemic; increase uptake of seasonal vaccine in low and middle income countries

Production



GMP



NRAs



Logistic



Campaign



On time

Early begin of production and as much as possible

