

# Impfstoffe haben ihre Wirksamkeit bewiesen - Wird es genügend während der nächsten Influenza-Pandemie geben?

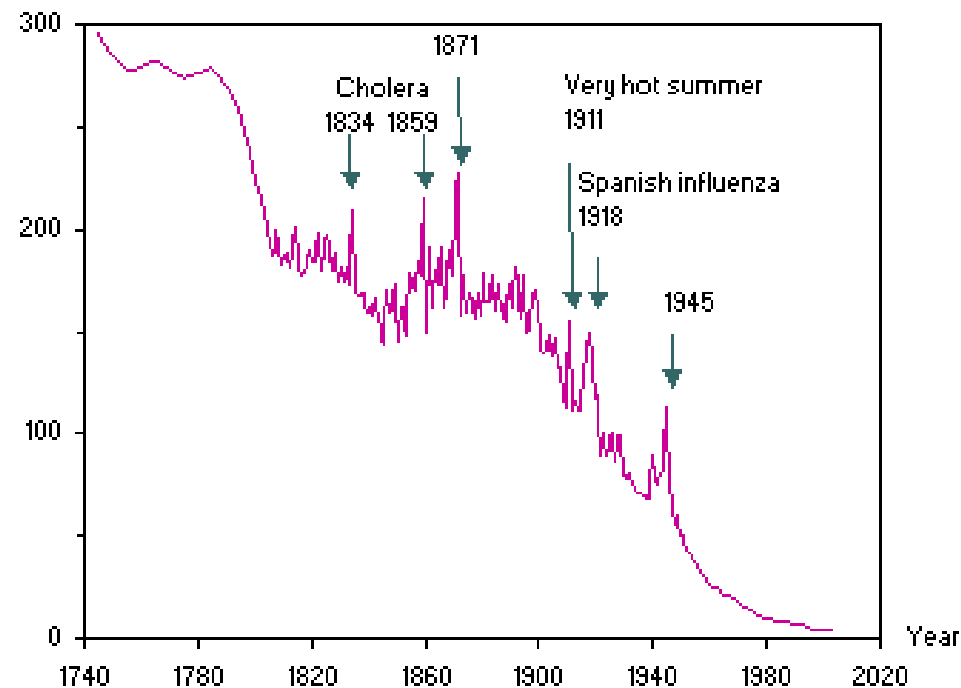
---

Prof. Dr. Klaus Stöhr  
Direktor Influenza Franchise  
Novartis Vaccines and Diagnostics

# Vaccines are major driver in reducing disease and death in children

## Infant mortality in France : 1740-2004

Risk of a newborn dying before his/her first birthday  
(per 1,000 live births)



Source : Gilles Pison, *Population and Societies* n°410, Ined, march 2005

Teaching Kit, Ined ([www.ined.fr](http://www.ined.fr))

\*Source: WHO fact sheet 288 'Immunization against diseases of public health importance'

\*\*Source: The Independent (UK), January 19, 2007

Globally, 75% of children are immunized with basic vaccines

- saving more than three million lives annually and preventing disabilities in 750,000 children

# Mit Impfstoffen verhütbare Erkrankungen

Häufigkeitsvergleich 20Jh. und 2006

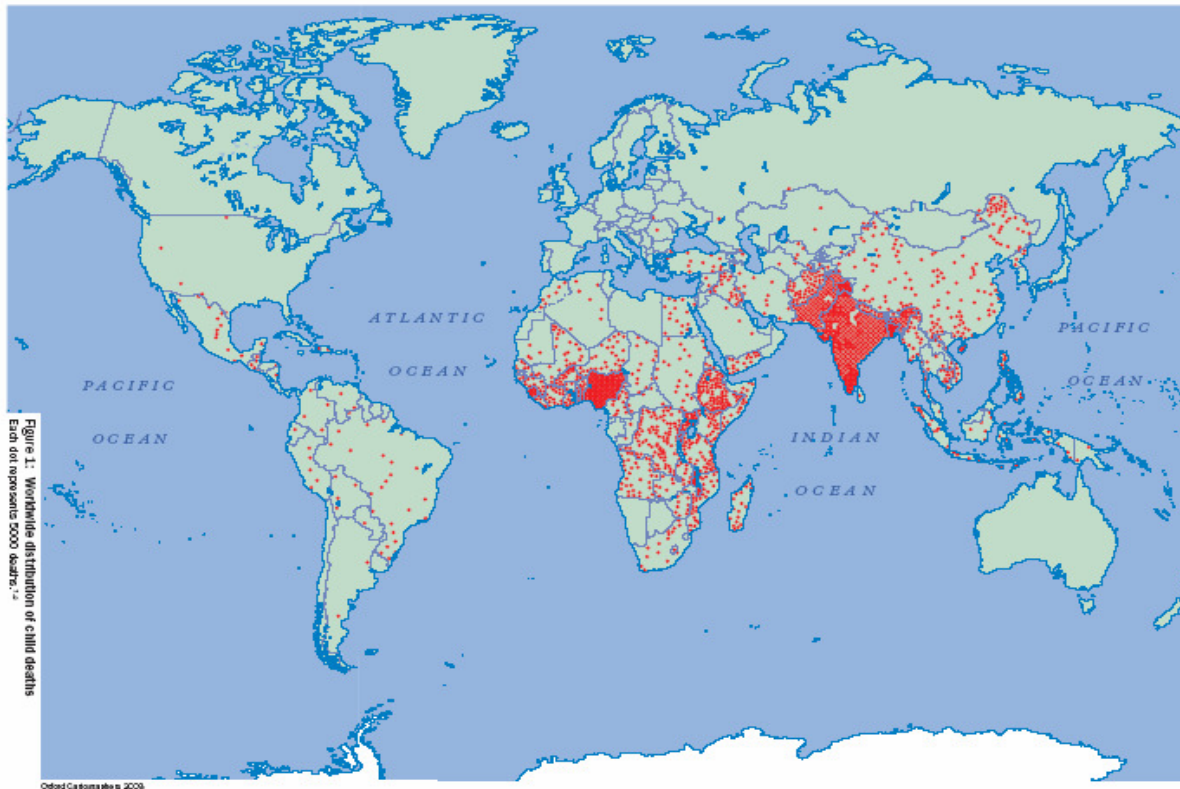
## Vaccine-Preventable Diseases US

Disease	20th Century Annual Morbidity	2006	Percent Decrease
Smallpox	48,164	0	100%
Diphtheria	175,885	0	100%
Measles	503,282	55	>99%
Mumps	152,209	6,584	96%
Pertussis	147,271	15,632	89%
Polio (paralytic)	16,316	0	100%
Rubella	47,745	11	>99%
Congenital Rubella Syndrome	823	1	>99%
Tetanus	1,314	41	97%
<i>Haemophilus influenzae</i> type b and unknown (<5 years of age)	20,000	208	99%

Sources: CDC, *MMWR* April 2, 1999. 48:242-264 and August 24, 2007/56(33):851-863

# 10.5m early childhood (<5y) deaths

>2 million are preventable by routine immunizations



Pneumococcal	28%
Measles	21%
Rotavirus	16%
Hib	15%
Pertussis	12%

World Health Report (Annex table 2, unpublished data for 2002) 2004 and the Lancet, 2003; 361:226-34.

# Warum wird es nicht genügend Influenza Impfstoff während der nächsten Pandemic geben?

---



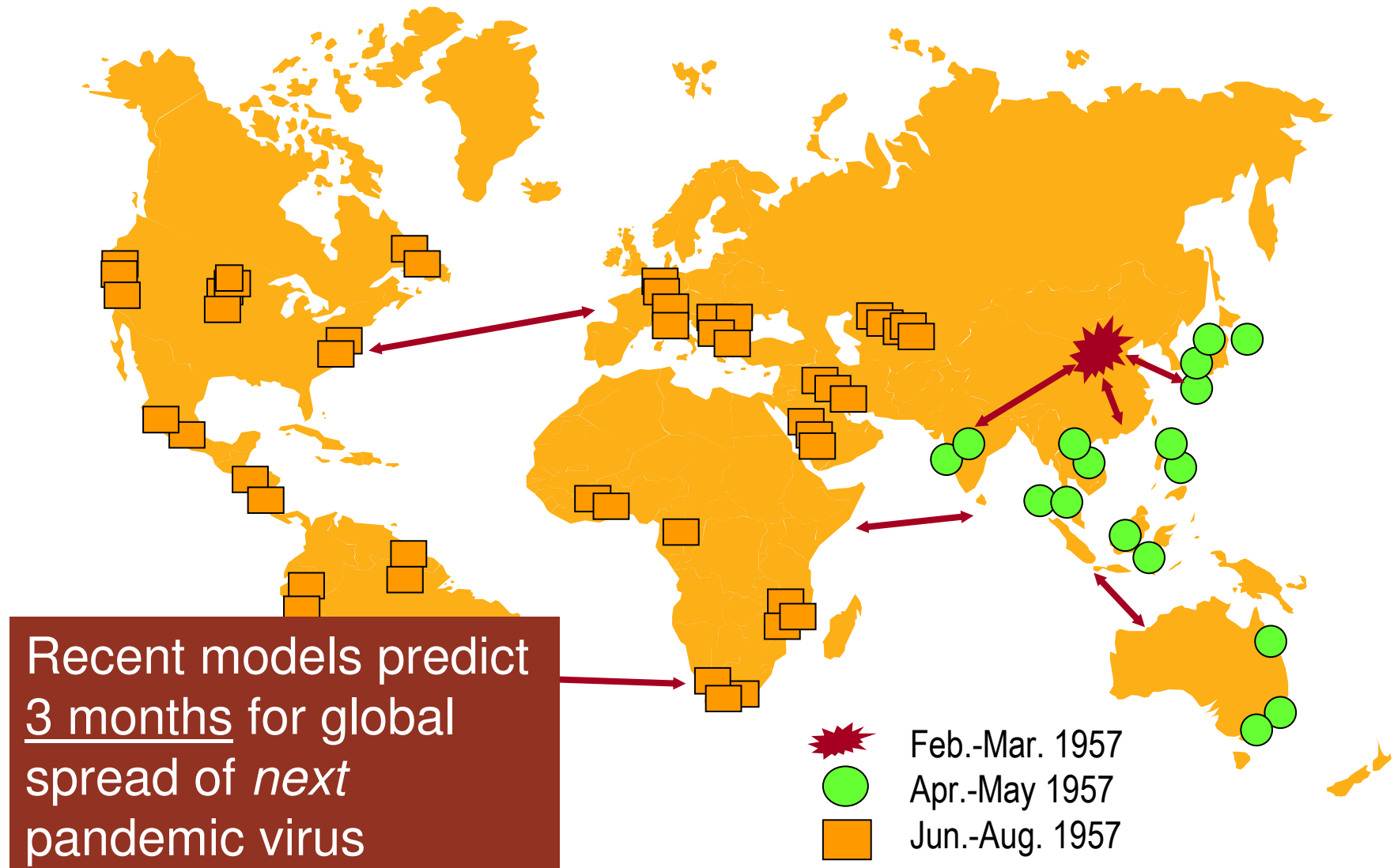
# Warum wird es nicht genügend Influenza Impfstoff während der nächsten Pandemic geben?

---

- Warum werden wir Impfstoffe benötigen?
- Wann/wie schnell nach dem Ausbruch wird er benötigt?
- Wer braucht Impfstoff?

# Global spread in 6 months 1957

## *H2N2 Asian influenza*



Global influenza vaccine production capacity is driven by influenza vaccine demand

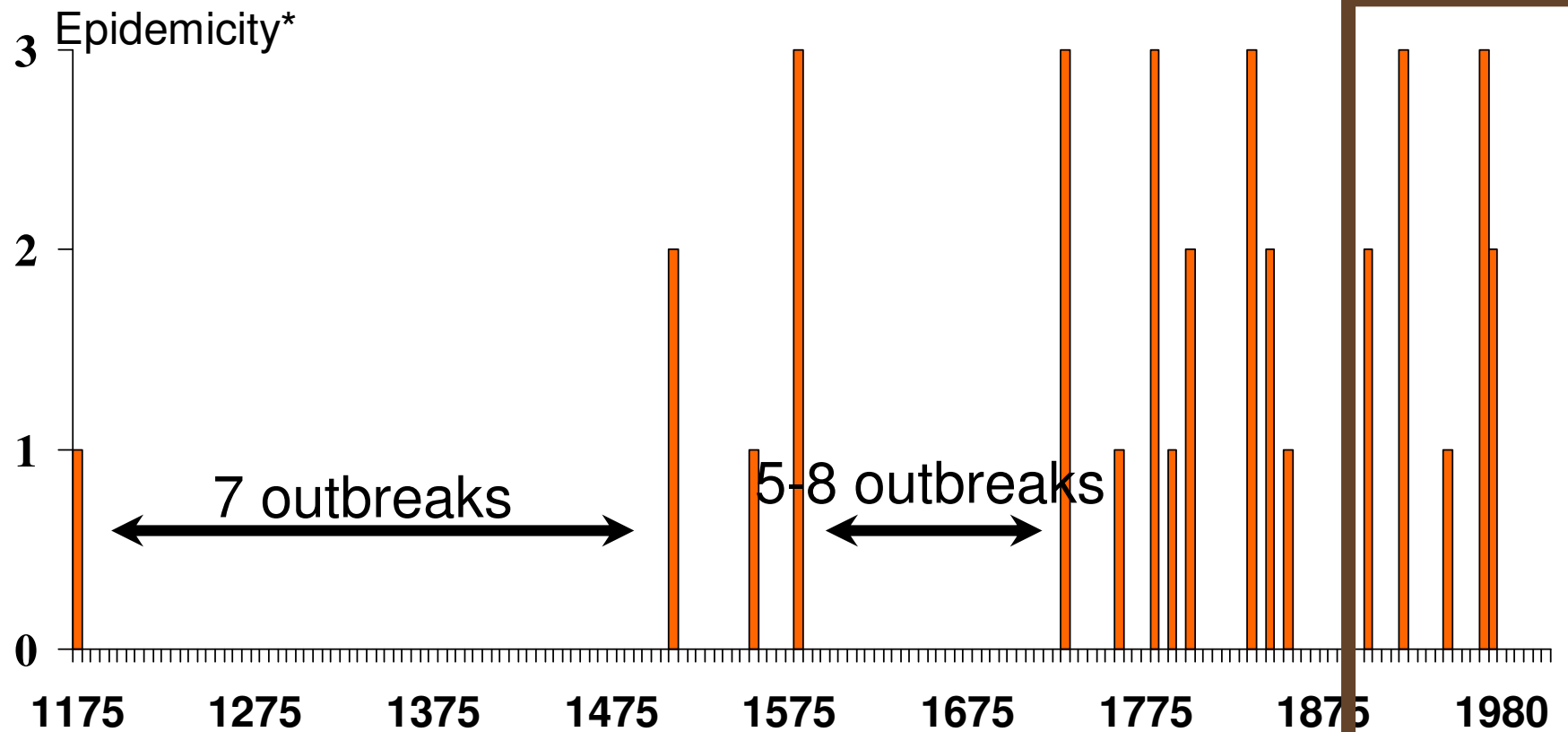
---

**World population**

**Seasonal influenza vaccine production/ up-take**

Estimated current global pandemic vaccine stockpile

# Recorded Influenza Pandemics\*

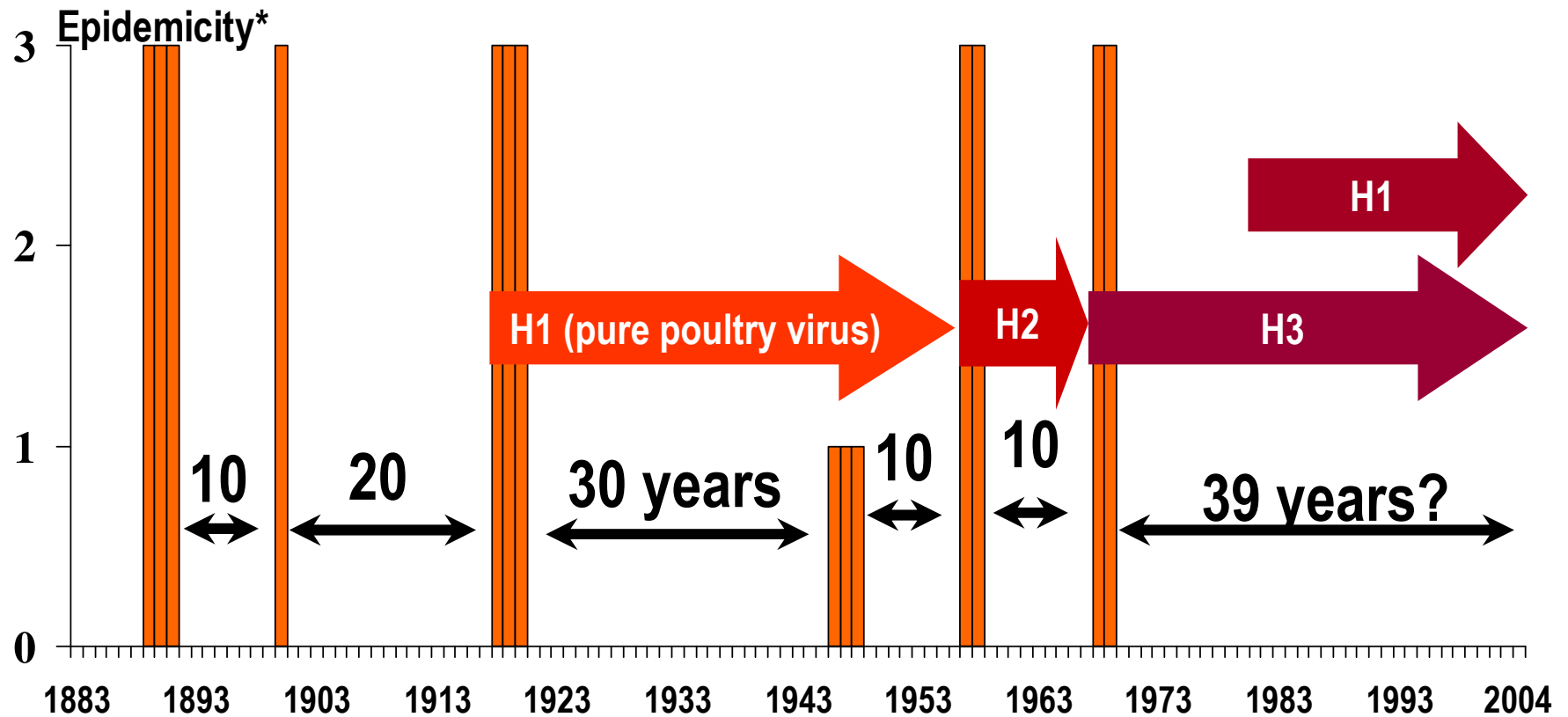


\* No laboratory evidence for events before 1888

1: epidemic, 2: probable pandemic, 3: pandemic

Potter, C.W: Textbook of Influenza by Nicholson, Webster, Hay, Blackwell  
Science 1998

# Recorded Influenza Pandemics



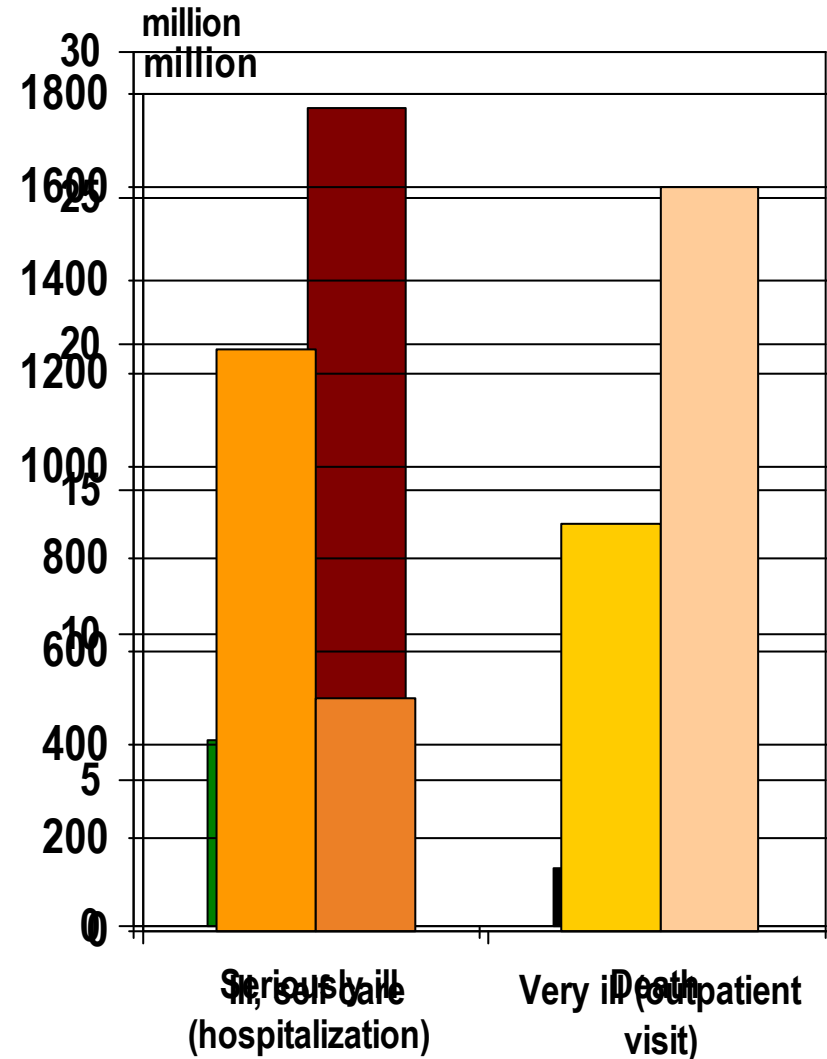
**1: epidemic, 2: probable pandemic, 3: pandemic**

Potter, C.W: Textbook of Influenza by Nichols, Webster, Hay, Blackwell Science 1998

# Influenza Pandemics: Why are we concerned?

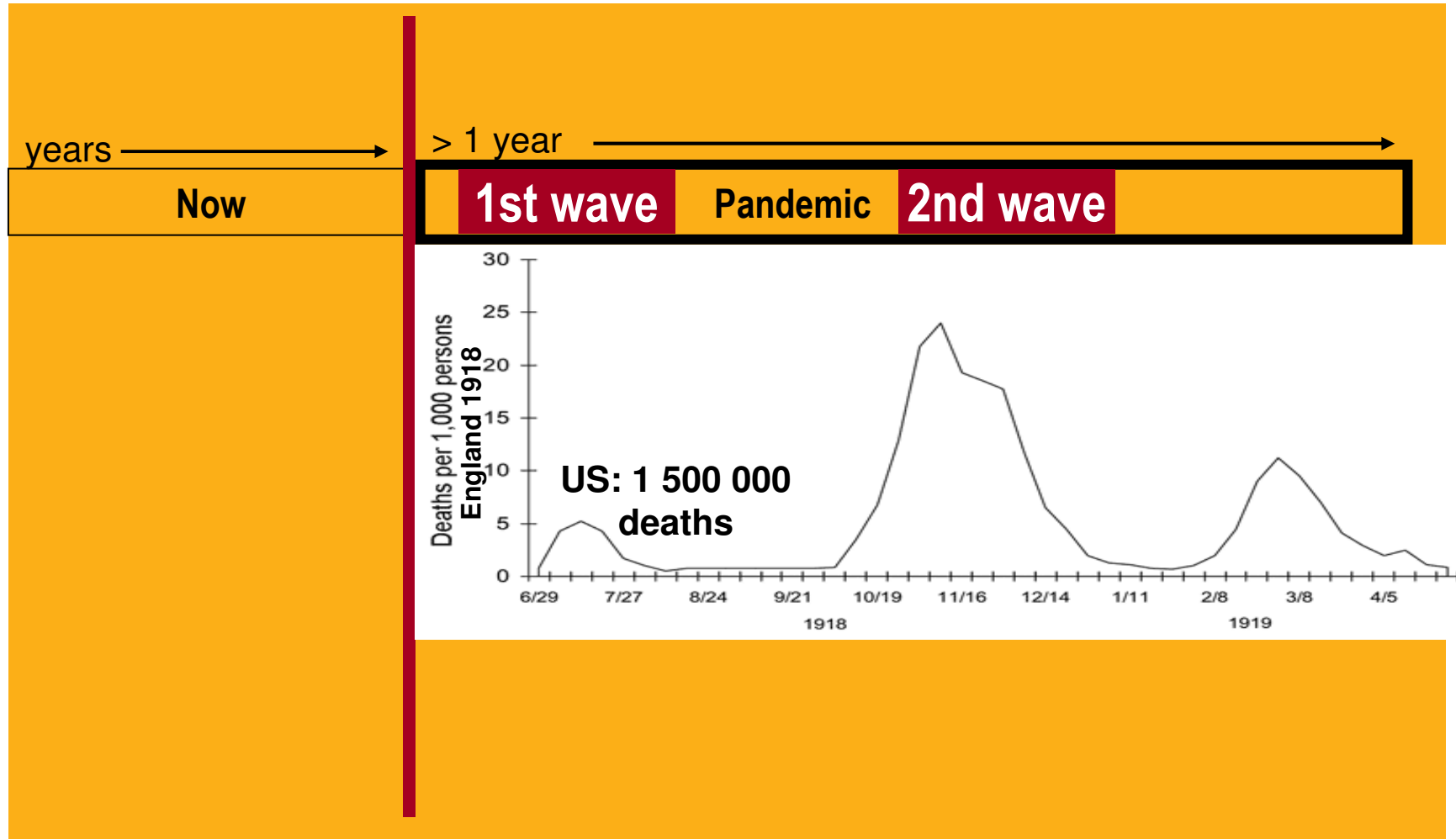
## Global Health Implications

- **Disease and death** (attack rate 35%)
  - 1253 - 500 million ill
  - 875 - 1601 require medical care
  - 6.4 - 28.1 hospitalizations
  - 2-7.4 million death
    - 0.03-0.12 % of global population
    - 1918: 1.25% (20 million death)
- **During few weeks**
- **Several waves**



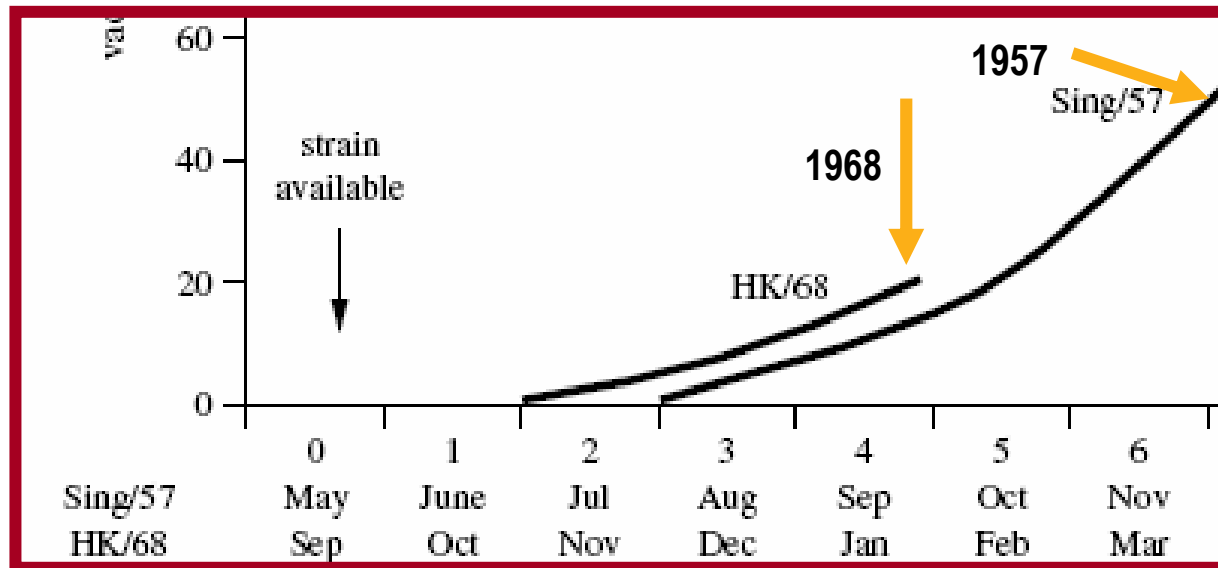
Extrapolated by Meltzer 2003 from Meltzer et al 1999

# Verlauf einer Influenza Pandemie



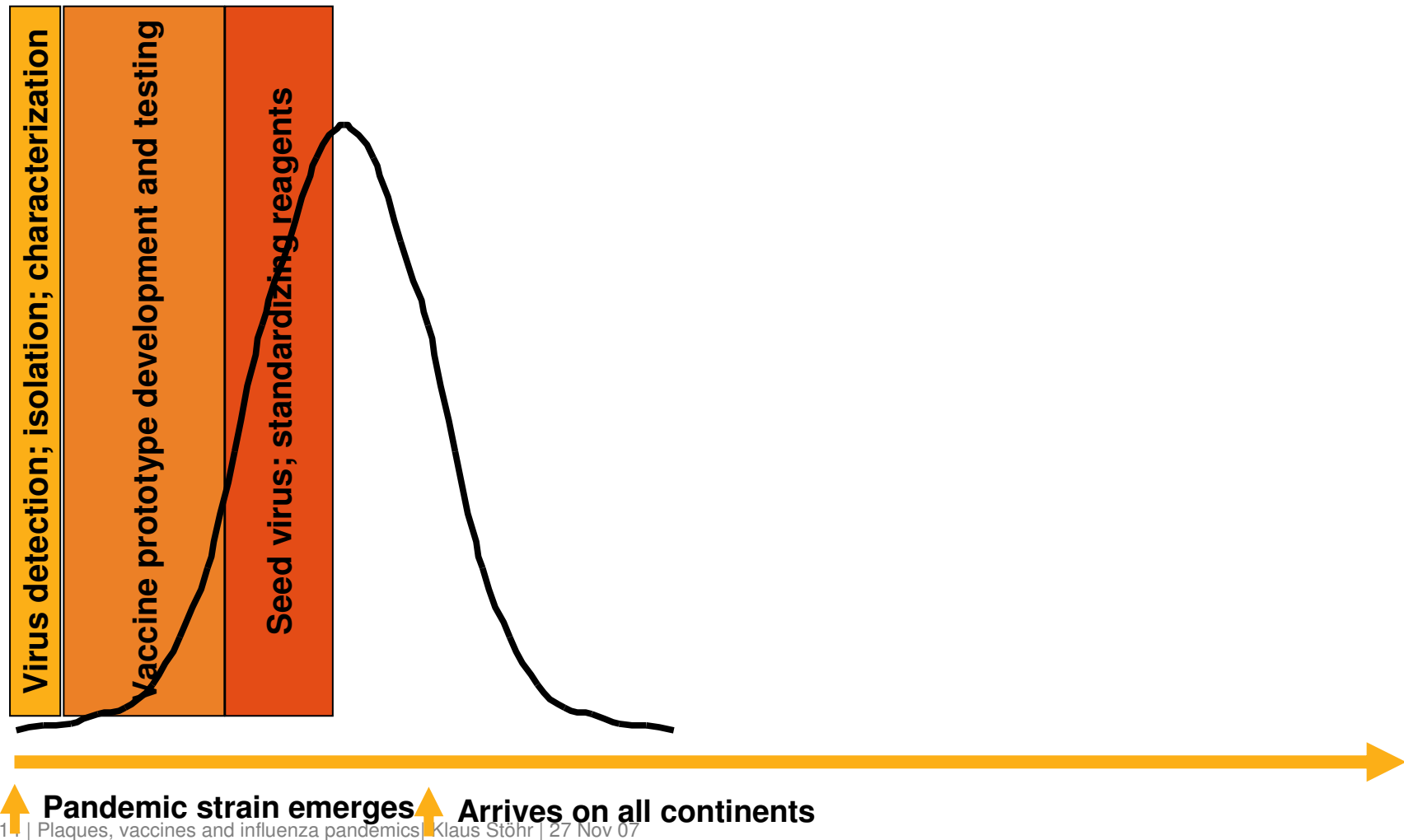
# Role of pandemic influenza vaccines DURING a pandemic?

- During last pandemics: vaccines played in-significant role
  - No warning on emergence and global spread too quick
  - Vaccine production began 1. too late, was 2. too small in volume and 3. could not be ramped up quickly

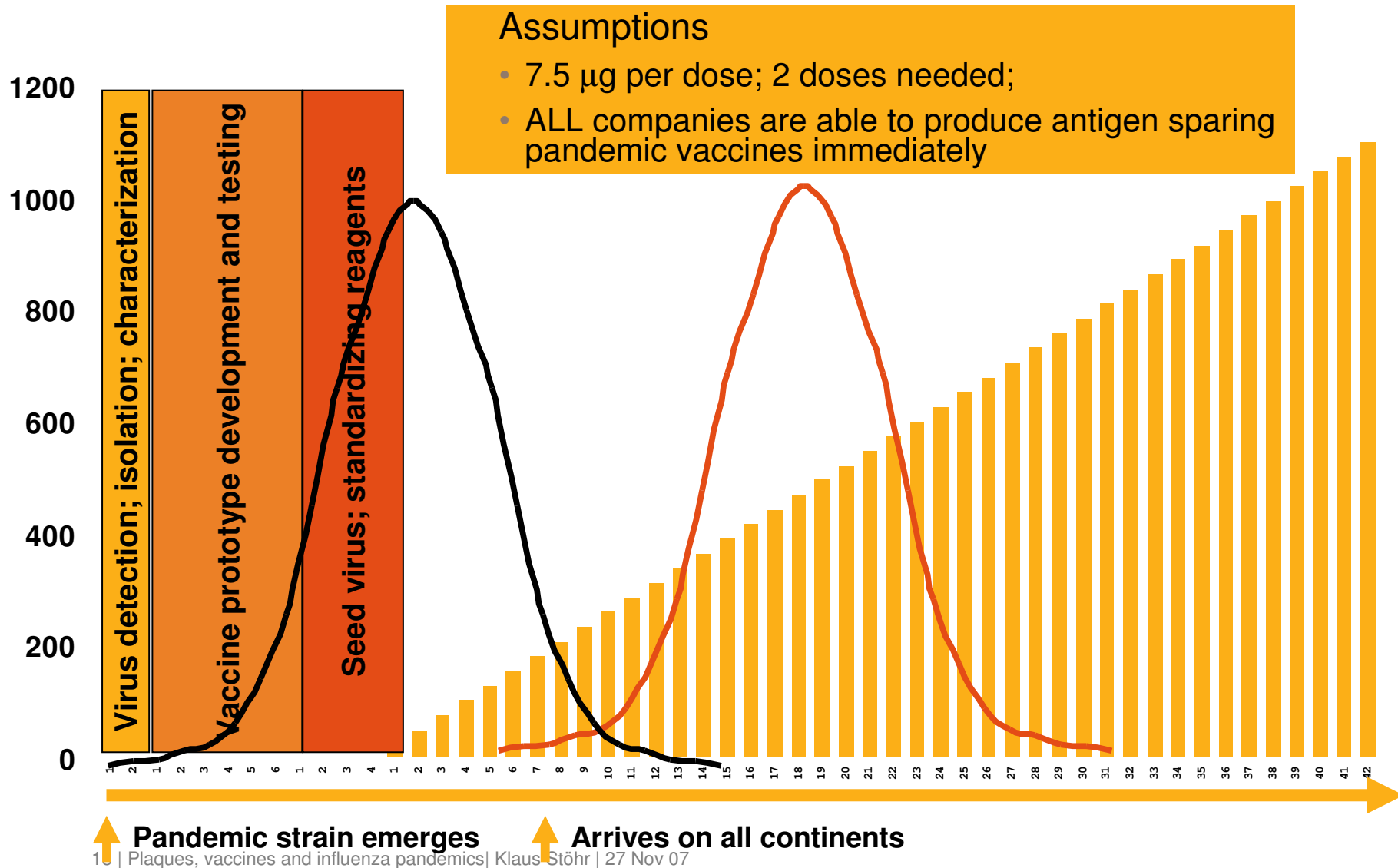


wood. *Trans R Soc Lond B.* 2001;1954ff

# Erste Welle wird einige Länder schon erreicht haben, bevor die Impfstoffproduktion beginnt



# Erste Welle wird einige Länder schon erreicht haben, bevor die Impfstoffproduktion beginnt



# Several **pandemic** vaccines have been licensed or are in development

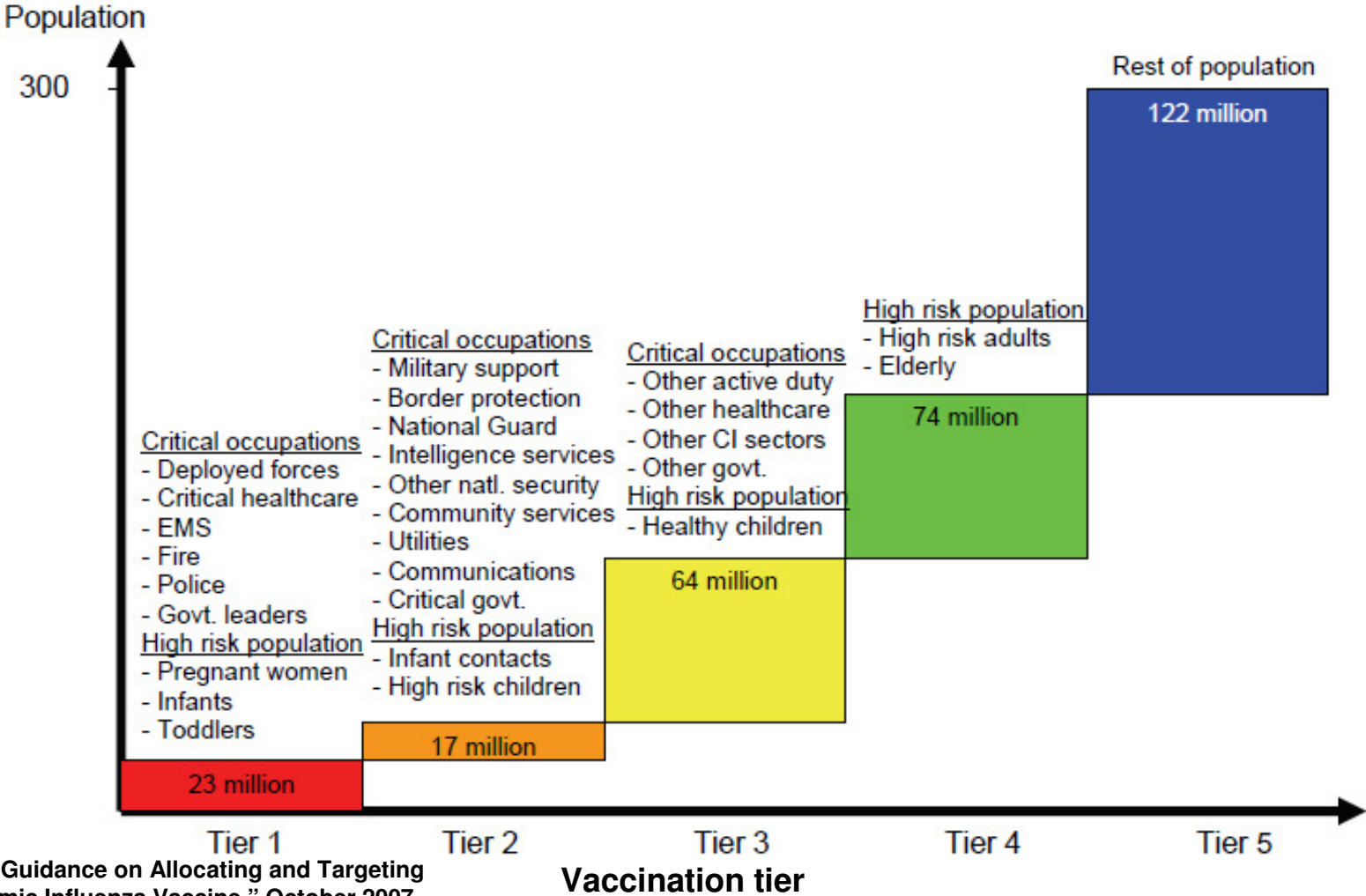
## Mock-up/Pandemic

Company	Strains	Regulatory status (EMEA)
Novartis	H9N2 & H5N3	EC approval (May 07)
Focetria	H5N1 (Split + MF59™)	Submitted Nov 06
GSK	H9N2 & H2N2	Submitted Dec 05
Daronrix	H5N1 (Whole + alum)	EC approval (March/07)
Pandemrix	H5N1 (Split + AS03)	Accepted for review (Jan 07)
Sanofi Pasteur	H5N1 (Split + alum)	Filing foreseen Q3 07

USA: SP split non-adjuvanted H5N1 pandemic vaccine stockpile approved by FDA (90 µg)

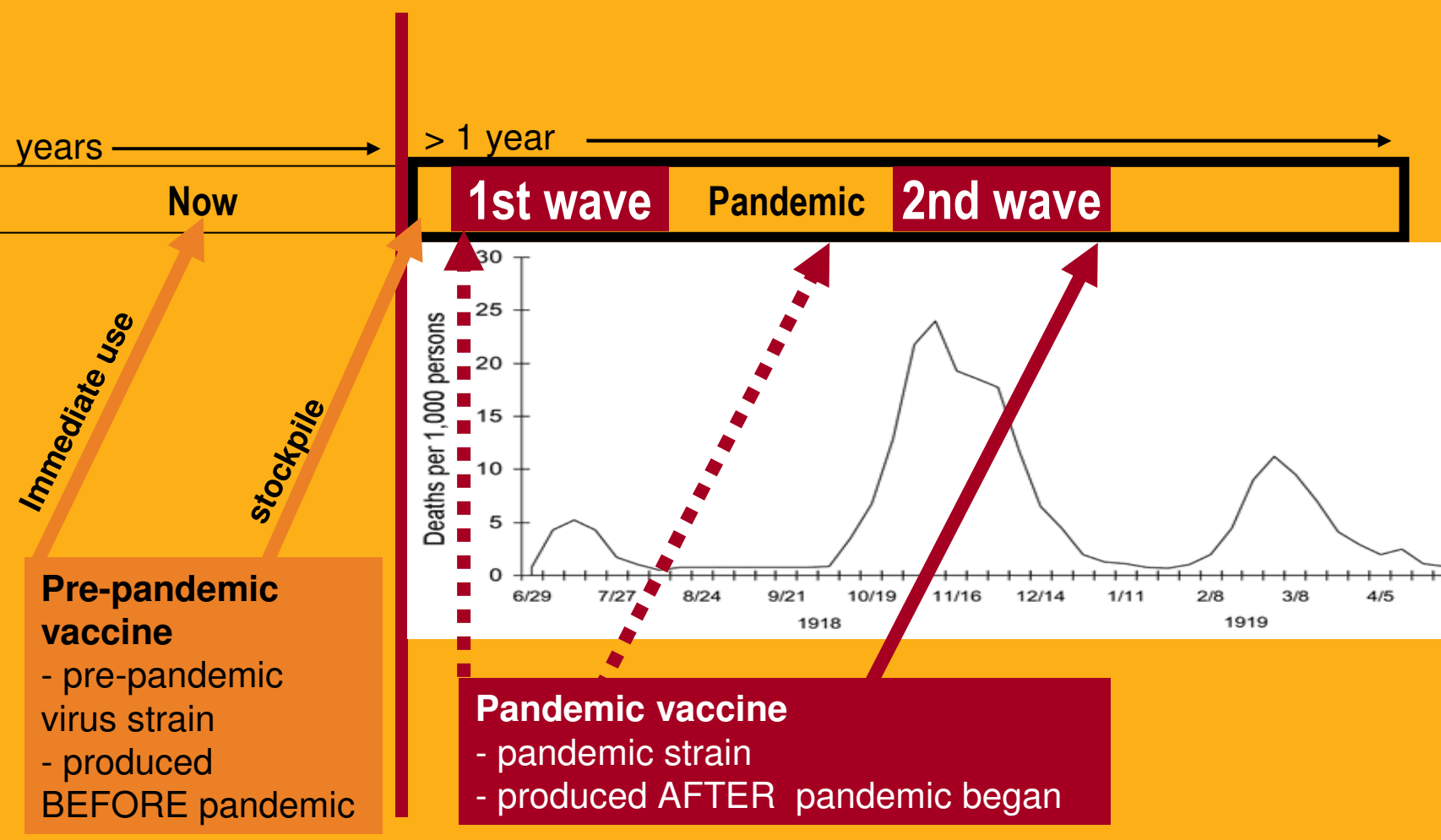
# Vaccination tiers and target groups for a severe pandemic: US Government Draft Guidelines Oct 07

- Vaccination is administered by tiers balancing vaccine allocation to occupationally defined groups, high-risk groups and general population

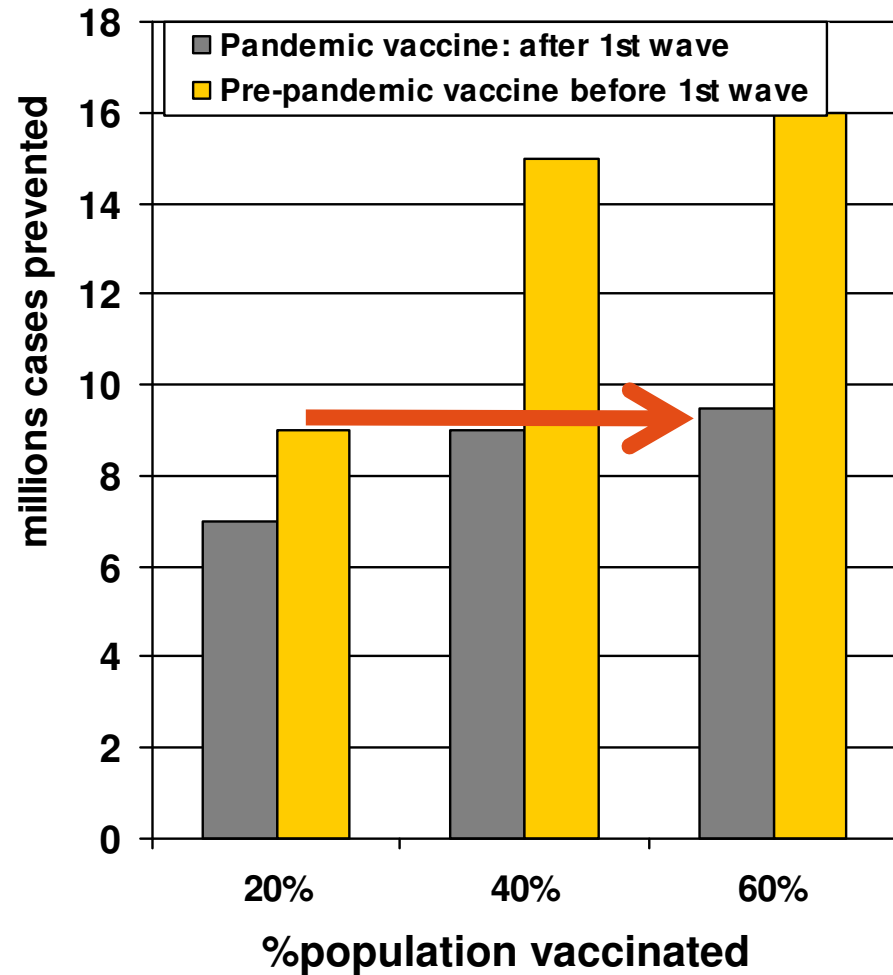


“Draft Guidance on Allocating and Targeting Pandemic Influenza Vaccine,” October 2007

# Pandemie-impfstoffe kommt für viele zu spät: gibt es Alternativen?



# Impfung gegen das Pandemie-virus: Erfolg hängt davon ab, WANN geimpft wird *UK model*



- Impfung von 20% der Bevölkerung VOR der Pandemie könnte einen ähnlichen Nutzen haben with die Impfung von 60% der Bevölkerung NACH der ersten Pandemiewelle.

Vynnycky et.al.IVW Vienna 2006

# Zulassung von pre-pandemischen Impfstoffen steht bevor

---

Company	Type	Regulatory status
<b>Novartis</b>	MF-59 adjuvant	<b>EMA final review ongoing; approval expected Q1-2 08</b>
GSK	AS03 adjuvant	Accepted for review by EMA Jan 07
BIKEN	Alum-adjuvant	PMDA licence within 2007
KITASATO	Alum-adjuvant	Completed the review by PMDA Aug. 07) Licence within 2007
Kaketsuken	Alum-adjuvant	MHLW submission (Dec. 07)
Denka Seiken	Alum-adjuvant	Submitted to MHLW (Jan. 07)
Baxter	No adjuvant	Submission planned early 2008

# Two possible uses of pre-pandemic vaccines

## *Stockpiling or immediate use*

---

- Stockpiling
  - Enables use after pandemic virus has emerged and before pandemic vaccine production can begin (>3-4 months)
- Governments have adopted this strategy (e.g. Australia, Europe, Japan and USA)
- Several companies have supplied H5N1 pre-pandemic vaccine: stored in bulk (big containers)
  - filling capacity into vials or syringes may be rate limiting factor after pandemic virus emerged
  - Stockpiling: expensive; limited shelf-life

# Two possible uses of pre-pandemic vaccines

## *Stockpiling or immediate use*

---

- Will H5 cause the pandemic? → potential for no benefit
- Framework outlined to license safe and immunogenic vaccines
  - First might be available shortly
- What is certain?
  - If the same subtype is causing the pandemic: some level of protection (exact match can not be predicted; range can be wide)
  - Vaccination of 20% of population before first wave equally efficacious as vaccinating 60% with pandemic vaccine after first wave
    - Even pre-pandemic vaccine with 50% reduced efficacy would be beneficial

# Odds: it is unlikely that PANDEMIC vaccine will be timely available; even in most of the industrialized countries

---

- Influenza vaccine production capacity matches just annual demand
  - Currently around 350mio doses per year (~5% of the world population)
- No early delivery: it will take at least 3 months until production with pandemic virus is in full swing
- Rapid pandemic virus spread expected
  - 3 months after emergence of fully transmissible virus: cases on all continents



■ Globally: ~ 3-600 million doses 6 months after pandemic?

- Pre-pandemic vaccines are licensed and will become available shortly