

# **Pandemic Influenza A (H1N1) Vaccine Background**

**August 2009**



# Pandemic vaccine manufacturers

- Same as producers of licensed seasonal influenza vaccine in the US
  - **Novartis (45.7%)**
  - **Sanofi Pasteur (26.4%)**
  - **CSL (18.7%)**
  - **MedImmune (5.8%)**
  - **GSK (3.4%)**

# Vaccine options

- Inactivated or live
- With or without adjuvant
  - Pre-mixed or separate
- Multi-dose or single-dose
- FDA-licensed or Emergency Use Authorization (EUA)

# Vaccine options

- Unadjuvanted multidose vials\*
- Unadjuvanted p-free pre-loaded syringes†
- Nasal sprayers (live attenuated)†

## Potentially

- Multidose vials pre-formulated with adjuvant
- Multidose vials formulated for adjuvant to be mixed at the place of administration (separate antigen and adjuvant vials)

\*All multidose vials will contain thimerosal preservative

†Up to 20% of vaccine may be p-free pediatric formulation

# Licensed vs. Emergency Use Authorization

“... use of an unapproved medical product or an unapproved use of an approved medical product during a declared emergency ...”

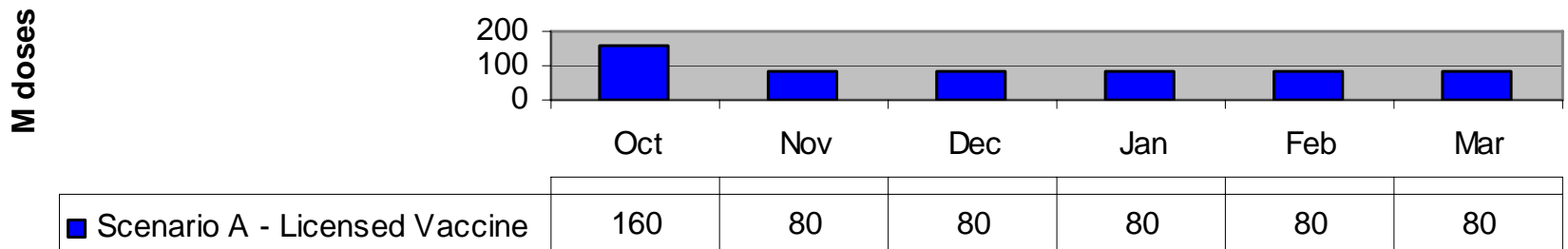
- **Unadjuvanted pandemic H1N1 vaccine may be licensed in a manner similar to a seasonal flu vaccine strain change and therefore would not need an EUA**
- **Adjuvanted vaccines, if used (for the 2009-10 flu season), will be administered under an EUA**

# How much?

- CDC vaccine projections after 13 weeks of delivery, applied to California
- Minimal: 13 Million doses
- Moderate: 27 M
- High: 45 M
- (Universal): (74 M)
- Annual seasonal influenza vaccine: ~12 M
- 1976 Swine flu: 40 M doses in US

# When?

## U.S. H1N1 Vaccine production projections: Unadjuvanted vaccine



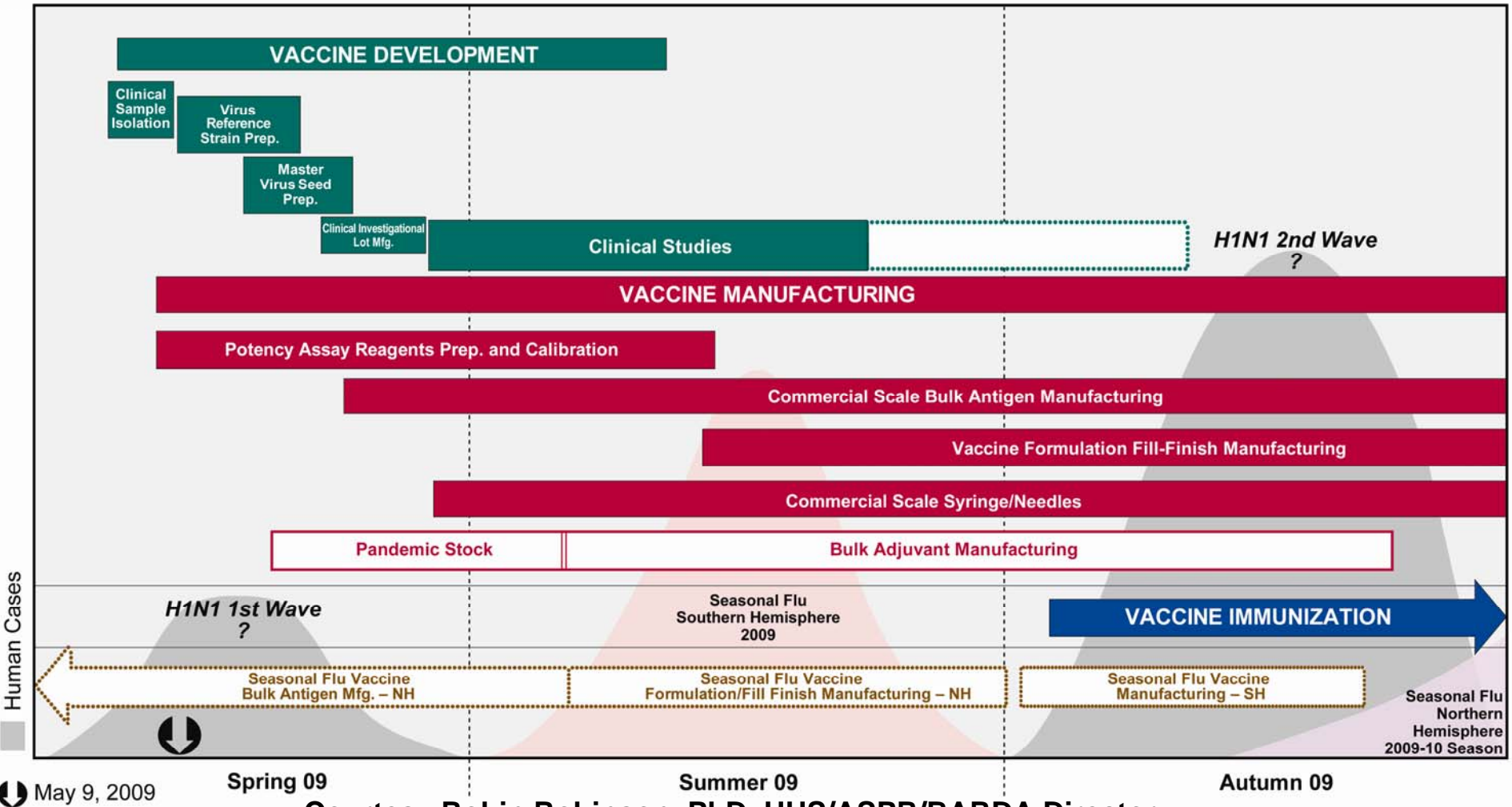
# Vaccine development

- Vaccine reference strain development
- Master seed strain preparation
- Clinical investigational lot manufacturing
- Clinical studies
  - To assess immunologic response and safety
  - Will inform formulation decisions

# Clinical trials to clarify...

- One or two doses
  - Elderly with immune memory?
  - Effect of adjuvant, or of live vaccine?
- 3 week interval between doses
- Amount in dose
- Local reactions, adverse events

# U.S. 2009-H1N1 Vaccine Strategy



Courtesy Robin Robinson, PhD, HHS/ASPR/BARDA Director

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- **No cost to immunizers for**
  - Vaccine
  - Shipping
  - Syringes, needles, disposal (sharps) boxes
- **Reimbursement**
  - Private insurers have stated intention to reimburse
    - (AHIP)
  - Medi-Cal and Medicare administration fees
  - Public clinics?

# Refrigerated @ 2-8°C

- Inactivated vaccine
- Live attenuated
- Oil-in-water adjuvant
  - 2-5 year shelf life
  
- Inactivated vaccine mixed with adjuvant
  - Stable up to 8 hours after mixing

# Distribution

- At least one private distributor to ship vaccine in California
  - Similar to VFC program
- Ordering and dose tracking systems
  - Web-based
  - Which elements of seasonal system?

# Lessons from Seasonal Influenza

- Demand vs. Supply?
  - Demand higher with initial release
  - Demand higher with perceived threat
  - When supply limited, scarcity followed by glut as demand quickly tapers off
    - Rationing raises risk of missed opportunities

# **ACIP 07/29/09**

- Who should be vaccinated?**
- Vaccination is recommended for any person 6 months of age or older who wants to reduce the risk for becoming ill with novel influenza A(H1N1) infection or of transmitting it to others**

## **ACIP - Target population groups that should be initial focus of immunization efforts**

- All children 6 months - 18 years of age (78M)
- All pregnant women (4M)
- Health-care & emergency services personnel (10M)
- All persons aged 19 - 64 years with medical conditions associated with a higher risk of severe influenza (34M)
- All household contacts of children younger than 6 months of age (4M)
- **Doses needed for 50% 2 dose coverage of primary target groups = 130 million doses**
  - Seasonal influenza vaccine coverage in these groups is only 20-50%

# ACIP – If supplies scarce...

- **While vaccine availability is very limited, subgroups within target groups that should be prioritized where feasible are**
  - Children aged 6m-4y
  - HCP/EMS
  - Pregnant women
  - Children with chronic medical conditions
  - Household contacts of infants <6m old

# ACIP Workgroup Recommendations

- **When vaccine availability increases to the point that ample supply at the local level is available to routinely vaccinate initial target populations, vaccination against novel influenza A(H1N1) is recommended for healthy adults aged 19-64 years old**
- **Vaccination of persons aged 65 or older is recommended once ample vaccine is available to routinely vaccinate all persons and vaccination programs are capable of meeting demand for vaccination from younger age groups**
  - **Vaccination with seasonal vaccine remains a high priority for persons aged 65 or older**

# Closing

Daunting challenge requiring public and private sector collaboration

- Harness existing infrastructure for seasonal flu vaccine
  - Seasonal flu: private >> public
  - Administration, distribution, ordering
- Filling in the gaps
  - New public and private providers
  - Ancillary staff – paid and volunteer

# Closing - Lessons to be learned...?

- How to achieve high influenza immunization rates in children?
  - Effect on transmission?
- Preview - immunization during high-lethality pandemic

# **Pandemic Influenza A (H1N1) Antiviral medication guidance**

[www.cdph.ca.gov/HealthInfo/discond/pages/swineinfluenza.aspx](http://www.cdph.ca.gov/HealthInfo/discond/pages/swineinfluenza.aspx)

**July 2009**



# **Pandemic Influenza A (H1N1)**

## **Oseltamivir resistance**

- **At least 5 cases detected since June**
  - Denmark
  - Japan (2)
  - Hong Kong ex California
  - Canada
- **At least 3 cases had been receiving oseltamivir to prevent infection after exposure**

# Oseltamivir resistance

## Testing at CDPH VRDL for

- **Adamantane resistance**
  - 59/59 (100%)
- **Oseltamivir resistance (sequencing)**
  - 0/251 (0%)

# Use of antivirals

## Balancing goals of

- Avoiding severe illness and death
- Accelerating antiviral resistance

## Considering current and future

- Influenza strains circulating
- How much flu-like disease is flu?
- Availability of vaccine
- National recommendations
- Hospitalization and death case data

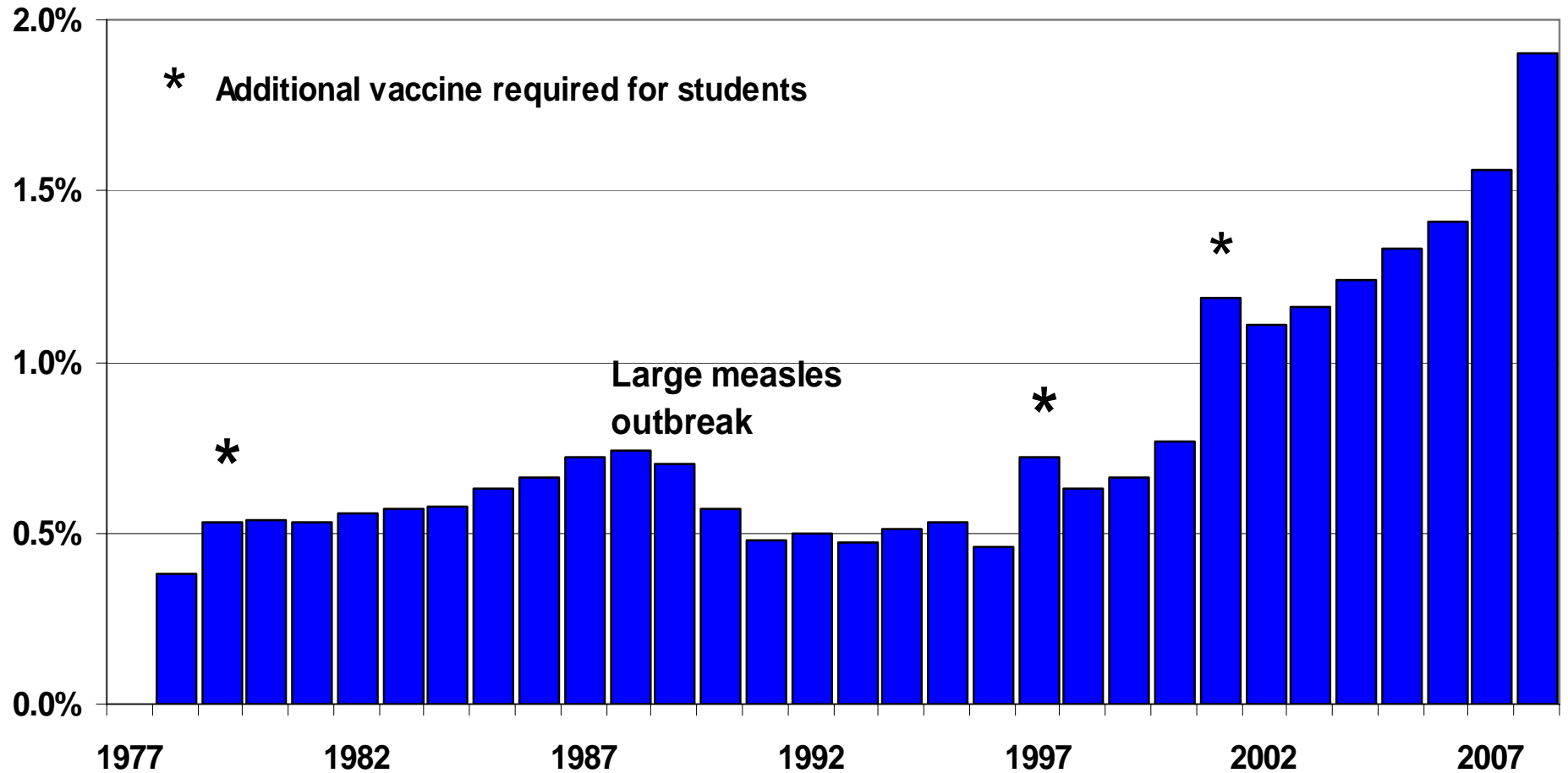
# Use of antivirals

## Hospitalization and death case data

Persons at higher risk for severe pandemic H1N1 virus infection have had:

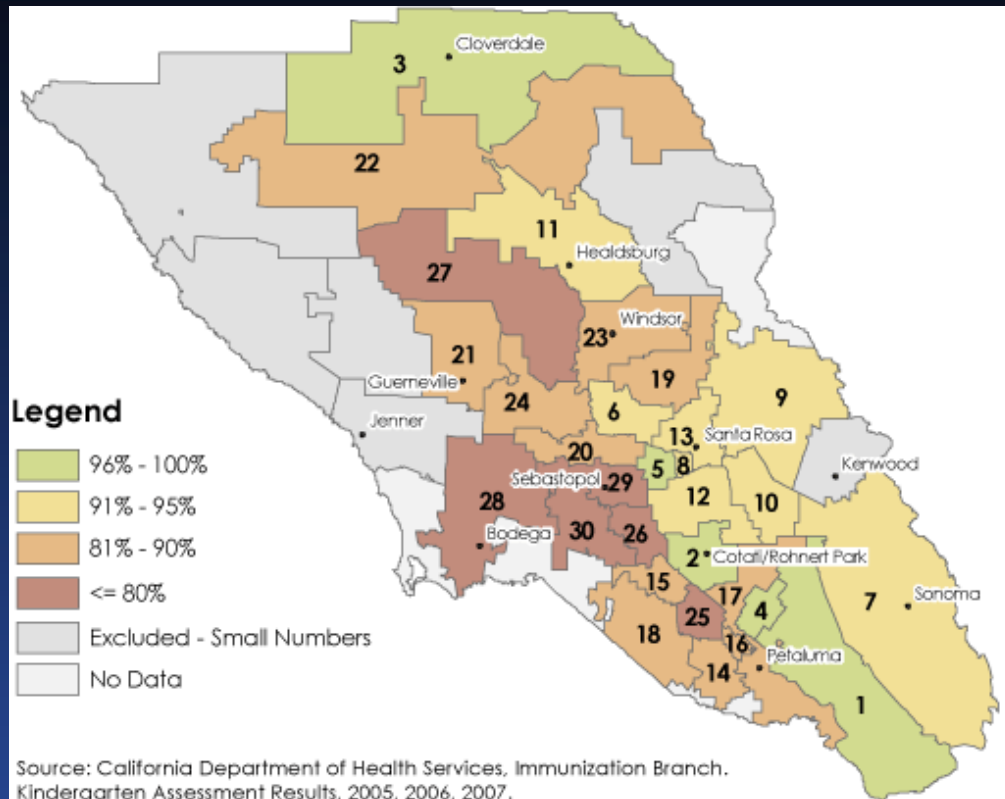
- Underlying medical conditions associated with severe seasonal influenza; OR
- A Body Mass Index (BMI)  $\geq 35$  (i.e., very obese).

# Percentage of Personal Beliefs Exemptions (PBE) Among Kindergarten Entrants, California 1977-2008





# Sonoma County PBE rates



## School Districts with 2005-07 Average of 96% - 100%

|   |                             |       |
|---|-----------------------------|-------|
| 1 | OLD ADOBE UNION ELEMENTARY  | 97.92 |
| 2 | COTATI-ROHNERT PARK UNIFIED | 97.34 |
| 3 | CLOVERDALE UNIFIED          | 96.52 |
| 4 | WAUGH ELEMENTARY            | 96.42 |
| 5 | WRIGHT ELEMENTARY           | 95.95 |

## School Districts with 2005-07 Average of 91% - 95%

|    |                                 |       |
|----|---------------------------------|-------|
| 6  | PINER-OLIVET UNION ELEMENTARY   | 94.78 |
| 7  | SONOMA VALLEY UNIFIED           | 94.07 |
| 8  | ROSELAND ELEMENTARY             | 93.99 |
| 9  | RINCON VALLEY UNION ELEMENTARY  | 93.96 |
| 10 | BENNETT VALLEY UNION ELEMENTARY | 92.20 |
| 11 | HEALDSBURG UNIFIED              | 91.87 |
| 12 | BELLEVUE UNION ELEMENTARY       | 91.74 |
| 13 | SANTA ROSA ELEMENTARY           | 90.95 |

## School Districts with 2005-07 Average of 81% - 90%

|    |                              |       |
|----|------------------------------|-------|
| 14 | WILMAR UNION ELEMENTARY      | 89.77 |
| 15 | DUNHAM ELEMENTARY            | 88.89 |
| 16 | CINNABAR ELEMENTARY          | 88.42 |
| 17 | PETALUMA CITY ELEMENTARY     | 86.51 |
| 18 | TWO ROCK UNION ELEMENTARY    | 85.88 |
| 19 | MARK WEST UNION ELEMENTARY   | 85.66 |
| 20 | OAK GROVE UNION ELEMENTARY   | 82.35 |
| 21 | GUERNEVILLE ELEMENTARY       | 82.14 |
| 22 | GEYSERVILLE UNIFIED          | 81.08 |
| 23 | WINDSOR UNIFIED              | 80.83 |
| 24 | FORESTVILLE UNION ELEMENTARY | 80.70 |

## School Districts with 2005-07 Average of <=80%

|    |                              |       |
|----|------------------------------|-------|
| 25 | LIBERTY ELEMENTARY           | 80.00 |
| 26 | GRAVENSTEIN UNION ELEMENTARY | 73.88 |
| 27 | WEST SIDE UNION ELEMENTARY   | 73.02 |
| 28 | HARMONY UNION ELEMENTARY     | 65.28 |
| 29 | SEBASTOPOL UNION ELEMENTARY  | 57.43 |
| 30 | TWIN HILLS UNION ELEMENTARY  | 53.73 |

# Recent disease outbreaks in schools with high PBE rates

- Measles (protective immunity level, 92-94%)
  - San Diego County, 2008
- Mumps (75-86%)
  - Nevada County\*, 2008
- Pertussis (92-94%)
  - Nevada County\*, 2006-07
  - Tuolumne County, 2008
  - Contra Costa County, 2008

# Response

- Monitoring PBE and disease rates
- Study of PBE records
- Increasing education and outreach
- Reviewing PBE legal and policy options
- Registries can assist schools and public health in monitoring immunizations and controlling disease

# Outreach and education

## Comparative Risks, Disease vs. Vaccine

CIC and CDPH examples:

- Virtual town hall /webinar
  - “Vaccines: Wading through the confusion”
- “I Choose” campaign
- “Shot-by-Shot”
  - Testimonials by disease survivors
- Vaccine safety education for parents, health care providers



# Extras

# Vaccine products

- Novartis (45.7%)
  - Multidose vials: standard unadjuvanted
  - Multidose vials pre-formulated with Novartis MF59 adjuvant\*
- Sanofi Pasteur (26.4%)
  - Multidose vials: standard unadjuvanted and formulated for GSK ASO3 adjuvant (separate antigen and adjuvant)\*
  - P-free pre-loaded syringes

\*Decision to use an adjuvanted vaccine is TBD

# Vaccine products

- CSL (18.7%)
  - **Multidose vials: standard unadjuvanted and formulated for GSK ASO3 adjuvant (separate antigen and adjuvant)\***
  - **P-free pre-loaded syringes**
- MedImmune (5.8%)
  - **Nasal sprayers, p-free**
- GSK (3.4%)
  - **Multidose vials: standard unadjuvanted and formulated for GSK ASO3 adjuvant (separate antigen and adjuvant)\***

\*Decision to use an adjuvanted vaccine is TBD

- **ASO3 adjuvant**



# Treatment

- Antiviral treatment for five days is recommended for cases:
- Cases who:
  - Are hospitalized; OR
  - Are at a higher risk for severe influenza; OR
  - Have pneumonia.

# Treatment

- Prompt treatment is optimal, but beginning treatment more than 48 hours after onset of symptoms may still be beneficial and is also recommended.

# Treatment

- **Higher (e.g., double) doses and extended (e.g., up to 10 days) courses of treatment should be considered for patients:**
  - Requiring intensive care; OR
  - At higher risk (e.g., BMI >35) and either hospitalized or with pneumonia.
  - Outpatients at higher risk should be monitored closely for pneumonia.

# Chemoprophylaxis

- Antiviral chemoprophylaxis for  $\leq 10$  days after last exposure can be considered for:
  - Persons who are at high-risk for severe influenza and have been close (e.g., household) contacts of a case.
  - Healthcare workers or public health workers who were not using appropriate personal protective equipment during close contact with an infectious case. Most of these exposures can be prevented by infection control measures for healthcare settings.
  - Patients at high risk for severe influenza who have had close contact with an infectious healthcare worker or patient who is a confirmed or probable case.

# Use of antivirals

**These recommendations also apply to most educational, residential and correctional facilities, including most camps.**

**However, antiviral treatment and prophylaxis of residents and employees are recommended during outbreaks of confirmed pandemic influenza A (H1N1) virus infection in nursing homes and other facilities where persons at high risk of severe influenza receive medical care or reside for longer stays (e.g., intensive care or transplant units).**