




H1N1 Vaccines

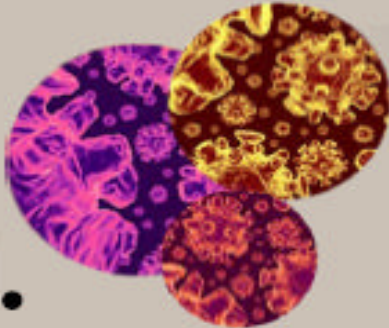
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Yearly Steps to Influenza Vaccine Identification and Distribution

1.

Worldwide influenza disease surveillance by the World Health Organization (WHO)



2.

FDA and WHO review data to recommend the composition of influenza virus vaccines for next winter's influenza season.



3.

Each February, FDA convenes its Vaccine and Related Biological Products Advisory Committee and recommends the three strains of influenza virus to include in the U.S. vaccine.



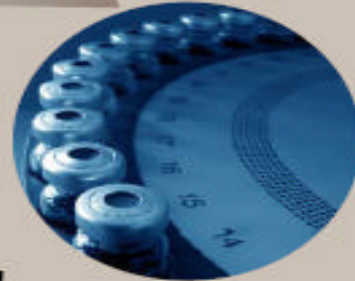
4.

The viruses are adapted for use in manufacturing.





6. Using reagents developed and calibrated by FDA, manufacturers and the FDA test their vaccine for potency and safety.



7. Vaccine is formulated into standard dosages, and is filled and finished by the manufacturers into final containers such as vials, syringes, and sprayers.



5. U.S. licensed vaccine manufacturers obtain reference influenza viruses from WHO Collaborating Centers to generate the "seed virus" for further vaccine manufacturing.

8. Each vaccine set ("lot") must meet FDA's rigorous standards for safety and efficacy as it rolls off the manufacturer's production line.



9. FDA releases lots and the manufacturers begin shipping vaccine throughout the U.S. for use by the public.





Yearly Steps to Influenza Vaccine Identification and Distribution





H1N1 Vaccines Clinical Trials in 2009-10

ClinicalTrial.gov
186 studies

CTRI 2010
9 studies



Approved Vaccines

Injectable, mono valent, subunit vaccine:

1. Glaxo smith kline Plc (GSK)
2. Baxter
3. Novartis
4. Sanofi Pasteur
5. CSL
6. Sinovac

Intranasal: Live attenuated

1. Medimmune



Approved Vaccines

Approved monovalent inactivated injectable vaccines (FDA)

Influenza A (H1N1) 2009 Monovalent Vaccine (ID Biomedical Co. of Quebec)[G
FDA approved for adults = 18 years old

Influenza A (H1N1) 2009 Monovalent Vaccine (CSL Limited) FDA approved for
adults > 18 years old and for infants and children = 6 months old

Influenza A (H1N1) 2009 Monovalent Vaccine (Novartis Vaccines and
Diagnostics Limited) FDA approved for persons > 4 years old

Influenza A (H1N1) 2009 Monovalent Vaccine (Sanofi Pasteur, Inc)
FDA approved for persons > 6 months old

MHRA (UK):

Pandemrix is pandemic influenza vaccine (H1N1)v
(split virion, inactivated, adjuvanted)

Celvapan is pandemic influenza vaccine (H1N1)
(whole virion, Vero cell derived, inactivated)



Approved Vaccines

Live attenuated intranasal monovalent vaccine (United States):

Influenza A (H1N1) 2009 Monovalent Vaccine (MedImmune LLC)
FDA approved for persons aged 2-49 years

single 0.2 mL dose for adults and children = 10 years old

two 0.2 mL doses about 1 month apart for children ages 2-9 years

each 0.2 mL dose given as 0.1 mL per nostril

live attenuated influenza vaccine is **not approved for use in pregnant women**



Vaccine Candidate strain (provided by WHO)

H1N1 monovalent Vaccine:

A / California / 07 / 2009 H1N1 like NYMC X-179 A

Grown in eggs (allantoic cavity, 72 hrs) → HA content measured

Gamma irradiated

Purity assessed (EU Pharmacopeia) limits <

1. Endotoxin 100 IU/dose
2. Ovalbumin 1000 ng/dose

Constituent of seasonal flu vaccine (3):

A / Brisbane / 59 / 2007 H1N1 like

A / Brisbane / 10 / 2007 H3N2 like

B / Brisbane / 60 / 2008 like

15 ug of HA of each virus



Indian Trials

1. Zydus Cadila: 8 Jan 2010 Phase 1
Open label, single treatment, single period, single dose
one IM dose of 15 ug of Haemagglutinin Antigen
adults (18 to 45 yrs), 20 + 4 sample size
44 days follow up
end points: 1. clinical safety, 2. immunogenicity after 21 days
2. Serum Institute of India : 7 Jan 2010 Phase 1
Live attenuated in adults, 0.5 ml intranasal, one dose
adults (18 – 49 yrs) 50, 60 days follow up
end points: 1. safety, 2. mucosal immunity
3. Sanofi Pasteur Bridging study Phase III
Single IM 100 adults 12 months follow up
Safety 7 days post IM, antibodies 21 days & 6 M



Indian Trials

4. Panacea Biotec 15 Jan 2010 Phase I
Three formulations strengths, two doses IM
72 adults, 85 days follow up
end points: 1. safety, 2. immunogenicity post dose day 21, 42

5. Panacea Biotec 15 Jan 2010 Phase II/III
3 formulations in pediatric patients (6 to 35 M)
360 children at 7 sites
95 days follow up

6. Panacea Biotec 15 Jan 2010 Phase II/III
3 formulations in children 3 to 9 years
360 children, 7 sites
95 days follow up

7. Panacea Biotec 30 March 2010 Phase II/III
3 formulations in adults, 5 sites
360 adults
95 days follow up



Indian Trials

- | | | |
|--|---------------|--------------|
| 8. Serum Institute of India | 25 Jan 2010 | Phase I |
| whole viron Inactivated vaccine in adults | | |
| 50 adults, one dose IM of 15 ug, | | |
| 60 days | | |
| 9. Serum Institute of India | 11 March 2010 | Phase II/III |
| adults multicentric IM, 0.5 ml on day 0 & 21 | | |
| containing either 10 or 15 ug | | |
| 10 sites, 330 volunteers | | |
| 120 days follow up | | |
| 10. Serum Institute of India | 15 Feb 2010 | Phase II/III |
| Live attenuated intranasal 0.5 ml on day 0 and 21 | | |
| Adults, pediatrics, elderly | | |
| 10 sites, 330 volunteers, | | |
| 120 days follow up | | |
| end point: 1. Safety; 2. Immune response on day 0, 21 & 42 | | |



Indian Trials

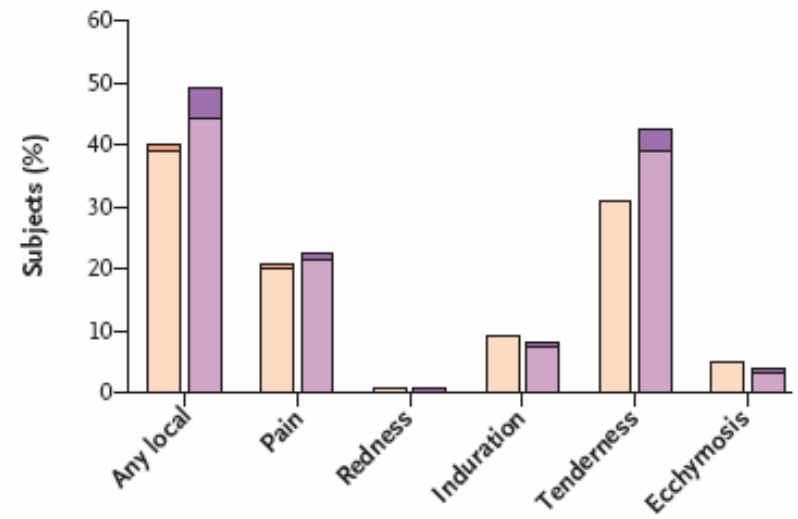
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|----------------------------|--------------|--------------|
| 11. Bharat Biotech | 2 March 2010 | Phase I |
| Inactivated IM Single dose | | |
| 160 adults | | |
| 60 days | | |
| 12. Zydus Cadilla | 2 March 2010 | Phase II/III |
| Inactivated IM | | |
| 6 sites | | |
| 120 days follow up | | |
| 200 volunteers | | |



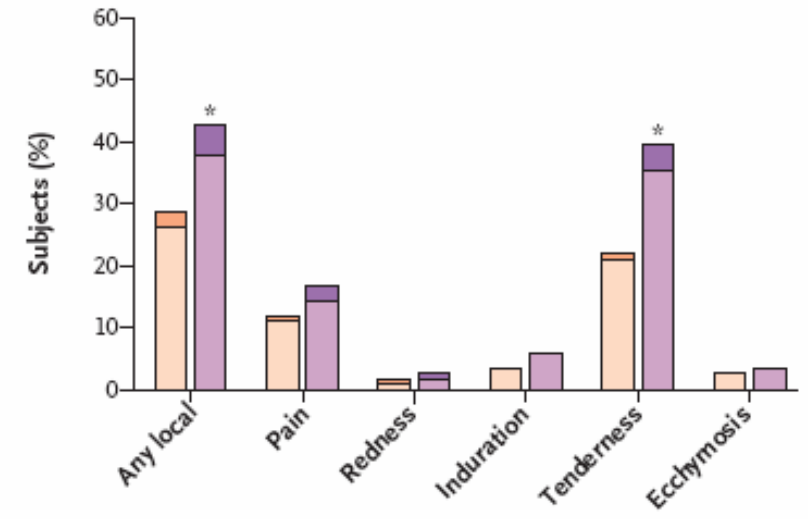
Safety Results

15- μ g Mild 15- μ g Moderate 15- μ g Severe 30- μ g Mild 30- μ g Moderate 30- μ g Severe

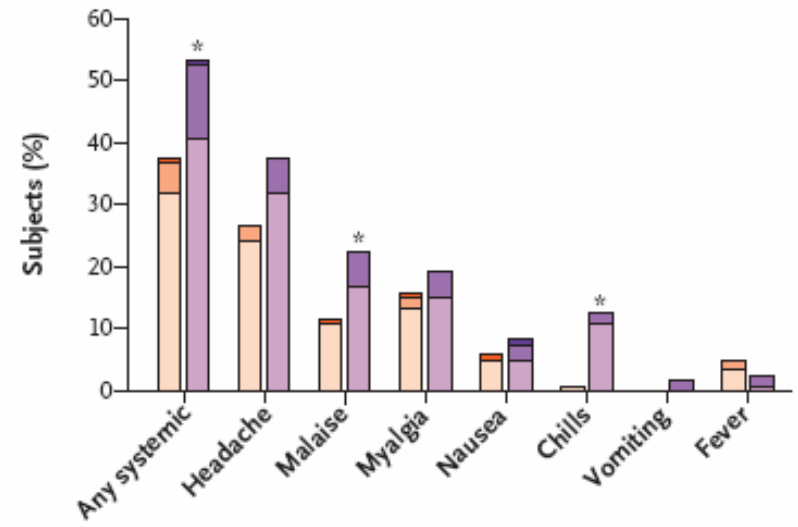
A Local Events after First Dose



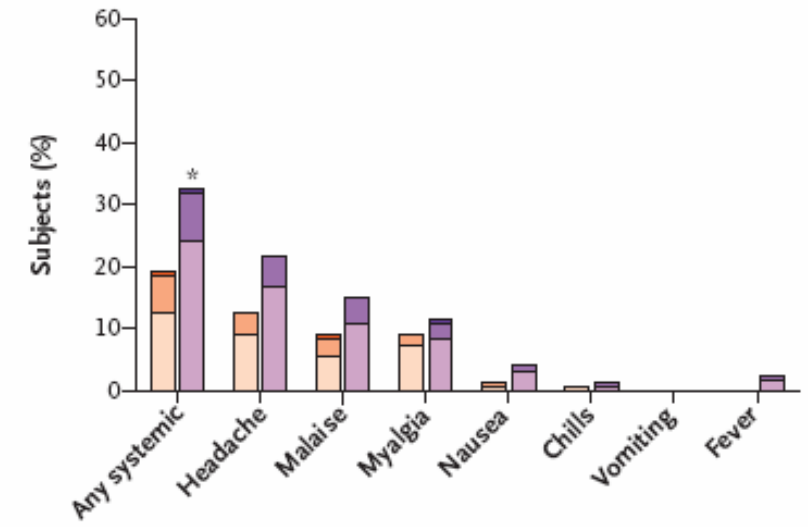
B Local Events after Second Dose



C Systemic Events after First Dose



D Systemic Events after Second Dose





Who should be vaccinated ?

1. Pregnant women
2. People who live with or care for infants < 6 months old
3. Health care and emergency medical services personnel
4. Persons aged 6 months through 24 years
5. People aged 25-64 years who have medical conditions that put them at higher risk for influenza-related complications
6. persons not in target groups may be vaccinated at provider discretion in consideration of local vaccine availability



Who should NOT be vaccinated ?

1. People who have a severe allergy to chicken eggs.
2. People who have had a severe reaction to an influenza vaccination.
3. People who developed Guillain Barre Syndrome within 6 weeks of getting an influenza vaccine.
4. Children less than 6 months of age (influenza vaccine is not approved for this age group), and
5. People who have a moderate-to-severe illness with a fever (they should wait until they recover to get vaccinated.)



Inactivated Vaccine Dosing:

single 0.5 mL dose for adults and children = 10 years old

two 0.5 mL doses about 1 month apart for children ages 36 months to 9 years

two 0.25 mL doses about 1 month apart for children ages 6-36 months

Live attenuated vaccine dosing for nonpregnant persons aged 2-49 years

single 0.2 mL dose for adults and children = 10 years old

two 0.2 mL doses about 1 month apart for children ages 2-9 years
each 0.2 mL dose given as 0.1 mL per nostril

pandemic (H1N1) 2009 influenza vaccine does not replace need for seasonal influenza vaccine