

Seasonal Influenza Vaccine Production Process

Seasonal influenza is an acute viral infection caused by an influenza virus. On average, each year in the U.S., more than 200,000 people are hospitalized from influenza complications, and 36,000 people die from influenza-related causes.

The processes sanofi pasteur employees use to produce influenza vaccines are regulated and approved by governmental health authorities. The first key step in vaccine production is the selection of a strain, or strains in the case of the seasonal influenza vaccine. Throughout the year, scientists from all over the world collect thousands of influenza virus samples and submit them to world health officials at World Health Organization (WHO) collaborating laboratories and the U.S. Centers for Disease Control and Prevention (CDC). Based on the analysis of dominant circulating strains, WHO and the FDA make strain recommendations for the annual influenza vaccine formulation.

WHO issues its recommendations for the Southern Hemisphere in September each year and in February, recommendations are made for the Northern Hemisphere. Following WHO action, the FDA makes its selection of the three viral strains to be included in the vaccine for the U.S. Once strains are selected, WHO reference laboratories distribute seed viruses to manufacturers to begin the production process.

Millions of specially prepared chicken eggs are used to produce the seasonal influenza vaccine. Throughout the year, eggs are delivered to sanofi pasteur and each one is injected with influenza virus; each virus strain is produced separately and later combined to make the final trivalent vaccine. The eggs are then incubated allowing the virus to multiply. After incubation, the virus-loaded fluid is harvested followed by multiple purification steps to ensure the virus is inactivated.

Quality control tests are performed on all batches for purity, sterility and potency in each step of the production process. Doses of the vaccine are formulated and filled in vials and syringes that must be properly packaged and labeled. Samples of every lot of formulated vaccine are sent to the FDA for release. Shipments of seasonal vaccines typically begin in August and continue into November, though virus yields and activity may lead to the additional release of doses into December and beyond.

Immunization may begin as soon as the vaccine becomes available and continues through the influenza season, which typically ends in March. Influenza immunity develops approximately two weeks following vaccination.

Seasonal Influenza Vaccine Production Process

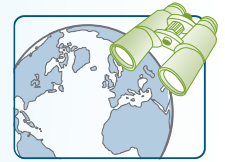
Surveillance

Year Round

- The seasonal influenza vaccine protects against the 3 most prominent virus strains circulating in a given year, which must first be identified before production can begin each year.
- Ongoing global surveillance is key to

predicting which 3 strains will circulate each influenza season.

- Scientists around the world submit samples to the World Health Organization and its reference laboratories, such as the Centers for Disease Control, which analyze and identify the circulating strains.

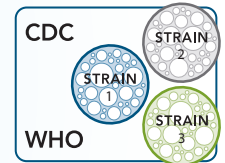


Strain Selection

January-March

- Based on the surveillance, WHO makes a strain recommendation in February for the Northern Hemisphere and in September for the Southern Hemisphere.

- In the U.S., the strains are submitted to the Food and Drug Administration (FDA) to recommend which 3 to include.
- WHO coordinates seed virus distribution.



Bulk Manufacturing and Production^{a,b}

January-July

- Millions of specially-prepared chicken eggs are used to produce the vaccine. Throughout the year, fertilized eggs are delivered to the manufacturer. Each egg is injected with 1 strain.
- Each virus strain is produced separately, and later combined to make 1 vaccine.

- The eggs are incubated for several days to allow the virus to multiply. After incubation, the virus-loaded fluid is harvested.

[Click here to see sanofi pasteur's Bulk Influenza Vaccine Manufacturing Process](#)

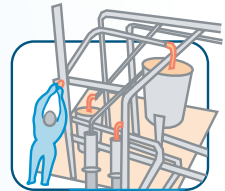


Purification and Testing^{a,b}

June-October

- The virus fluid undergoes multiple purification steps and a special chemical treatment to ensure the virus is inactivated, or "killed."^c
- The virus is split by chemically disrupting the whole virus.

- Manufacturers test the vaccine concentrate to determine amount and yield of the virus to ensure concentrate is adequate for immunization.

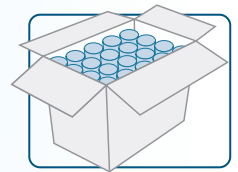


Formulation, Filling and Packaging

July-December

- Viral fragments from all 3 strains are collected from different batches, and combined upon completion of quality control tests.
- Quality control tests are performed on all 3 strains for purity, sterility and potency in each step of the production process.

- Manufacturers begin filling the doses into vials and syringes, which are then sealed and carefully inspected before labels are applied to show the vaccine batch, lot numbers, and expiration date.
- Each lot must be specifically "released" by the FDA before manufacturers can ship supplies.

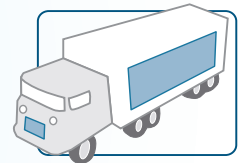


Shipping

August-November; Beyond as needed

- Vaccine shipments typically begin in August or September and continue into November.
- With the CDC's^d support, partial shipments are sent early in the season to all customers to ensure broad access for high-risk patients.

- Depending on viral yields and virus activity, additional doses may be released and distributed into December and beyond to support late-season immunization.

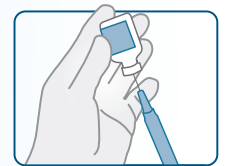


Vaccination

October and Beyond

- The CDC recommends an annual influenza immunization for anyone who wishes to reduce their risk of contracting influenza: children 6 months through 18 years of age; adults 50 years of age and older; pregnant women; and anyone with chronic health conditions such as asthma, chronic

- obstructive pulmonary disease (COPD), heart disease, and diabetes.
- Immunization may begin as soon as vaccine becomes available and continues through the influenza season, which typically ends in March.
- Immunity develops approximately 2 weeks following vaccination^e.



^aTo ensure safety and purity, vaccine is produced in a clean environment where quality control experts enforce strict standards, continuously monitoring the process; ^bThe majority of time for Bulk Manufacturing and Production and Purification and Testing is dedicated to testing and approval.; ^cThis process makes it impossible to contract influenza from the vaccine upon administration; ^dCenters for Disease Control and Prevention; ^eChildren younger than 9 years of age receiving vaccination for the first time need 2 doses 1 month apart.