Flu Cell Culture Manufacturing and the Novartis Proprietary Cell Line

Overview

Cell culture manufacturing is the first major innovation in inactivated influenza vaccine manufacturing in more than 50 years. It represents a new approach to vaccine production whereby influenza virus is propagated in readily available mammalian cell lines rather than in chicken eggs.

First major innovation in influenza vaccine manufacturing in more than 50 years

Virus cultivation utilizing the Novartis proprietary cell line as an exclusive host offers the possibility of more robust virus proliferation. Cell culture vaccine is produced in a closed bio-reactor system with readily available and standardized ingredients fully independent from animal-derived components. It also offers the possibility for vaccine seed strain development that more closely matches the original "wild" virus because cell culture technology eliminates the need for passage through eggs, where the virus may be forced to adapt in order to replicate. As a result, the vaccine antigen may prove more authentic to the wild type virus, potentially translating into a more immunogenic and effective vaccine.

Offers the possibility of more robust virus proliferation and more immunogenic and effective vaccines

More than 3,500 people received the Novartis cell culture-based vaccine which was used to validate the production facility during the clinical development program evaluating the vaccine's safety and immunogenicity. This data showed the vaccine fulfilled all of the EU's immunogenicity and safety criteria.

Novartis has an established vaccines business and is the only company that currently has cell-based vaccines manufacturing technology licensed in Europe. While cell-based production accelerates the vaccine manufacturing process, Novartis is also using egg-based manufacturing to increase the likelihood of the greatest possible vaccine supply.

Novartis is the only company with a licensed cell-based vaccines manufacturing facility

Advantages

The Novartis proprietary cell culture technology can enable flexible, faster start-up of vaccine manufacturing. With the introduction of cell culture derived influenza vaccines, Novartis Vaccines is

Contributing to meet the growing need for vaccines

contributing to meet the growing need for seasonal influenza vaccines and to quickly respond to potential pandemic influenza threats.

Results from a recent study show this cell culture-derived vaccine was comparable to conventional egg-based vaccines in stimulating an immune response as well as in its tolerability. The Novartis cell culture vaccine which was used to validate the production facility does not contain additives, such as antibiotics and thiomerosal. Additionally, people allergic to eggs and egg products can benefit from this vaccine since it is manufactured without egg proteins.

Five step production process

Simplified production process

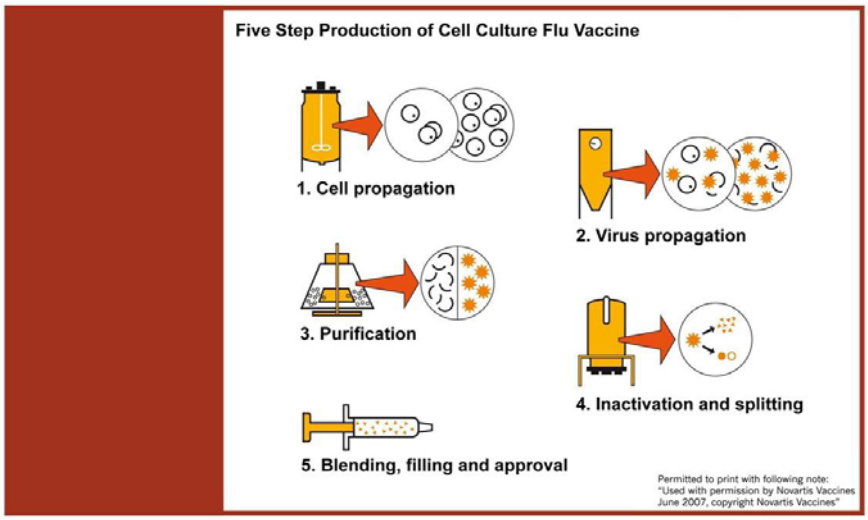
1. **Cell propagation:** Novartis proprietary cells grow in suspension, therefore they do not require attachment to a surface to proliferate. This simplifies vaccine production. During production, one ampule of stored cells is thawed and expanded in several steps. At each stage the cells are placed in fermenters (stainless steel tanks) that provide the optimal environment for growth including the proper temperature, pH value and nutrient solution. The proliferation of the cells is constantly monitored. Cell proliferation takes place in a contained fermenter system within so-called clean rooms.

2. **Virus propagation:** Once introduced, it takes the selected virus strain several days to multiply in the cells. During the course of this process, the viruses are released from the cells into the medium.

3. **Purification:** The first step in a long series of purification procedures known as separation, is where the virus–infected medium is separated from the cell debris. Viruses are then captured and separated from the medium solution.

4. **Inactivation and splitting:** Following purification, the virus is inactivated through a chemical process. Virus splitting follows because only fractions of specific viral surface proteins are required for the subsequent influenza vaccine. Further purification procedures are then performed. Since seasonal influenza vaccines contain three viral strains, the production process must be performed for each strain.

5. **Blending, filling and approval:** Once all purification procedures are completed, the vaccine is blended, filled and packaged. Final quality checks are performed, and the product is then released following regulatory approval and prepared for delivery.



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