

Crucell

Seasonal Influenza vaccine

March 2011

Crucell and sanofi pasteur reached an agreement on a series of transactions to restructure their long standing partnership. As part of the agreement sanofi pasteur returned to Crucell the commercial rights they held under an exclusive license agreement for the development and commercialization of a cell-based influenza vaccine (FluCell).

The exclusive license, agreed upon in December 2003, left Crucell with the marketing rights for FluCell in Japan only. With the return of the world-wide marketing rights, Crucell has commenced with the development of a cell-based influenza vaccine. The introduction of cell-based Inflexal® V will be the next important step for Crucell's respiratory franchise.

Combining Crucell's high density PER.C6® production system with the company's proprietary virosomal technology creates a cutting-edge method to produce Inflexal® antigens both at large scale, at very competitive cost levels and earlier in the season.

Influenza vaccines are classically produced on embryonated chicken eggs. The safety and efficacy of such vaccines is proven, but various challenges have led the biopharmaceutical industry and the scientific community to explore other ways of producing influenza vaccines. PER.C6® cells grow well in suspension and are easily scalable, potentially permitting the production of cost-efficient vaccines in large quantities. A key benefit of PER.C6® cells is that they have a safety profile that is unequaled by any other cell used for the manufacturing of influenza vaccines, such as African Green Monkey (VERO) cells and Madin Darby Canine Kidney (MDCK) cells. PER.C6® cells can produce all influenza strains that we have tested, both human strains and the avian strains that may present a pandemic threat.

Crucell expects to apply for licensure in 2014.

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About Influenza

Influenza, commonly called the flu, is a highly contagious infection of the respiratory tract that spreads from person-to-person through infectious respiratory secretion droplets caused by coughing or sneezing. Influenza outbreaks occur almost every year and their severity varies considerably. One unique aspect of influenza compared with other viruses, is its ability to continuously change over time, usually by mutation. This characteristic enables the virus to evade the immune system of its host, making people susceptible to the flu throughout their entire life. When infected with the virus, a person develops an antibody that works against that virus. Once the virus changes, however, the previous antibody is unable to recognize it, necessitating an entirely new antibody to fight off the virus. These modifications make it necessary for individuals to receive a different influenza vaccination each year, compared with one vaccination that would grant lifetime immunity.

Morbidity and mortality

Each year approximately 5-15% of the world's population contracts influenza and on average 3 to 5 million people suffer severe illness. An estimated 250,000 to 500,000 people die annually from influenza-related complications. Occasionally a major genetic shift in the influenza virus results in a deadly new virus strain to which the human population does not have immunity, and a global pandemic outbreak occurs. The Spanish influenza pandemic, the most severe outbreak of influenza to date, occurred from 1918 to 1920 and caused deaths worldwide ranging in estimation from 20 to 60 million. In 2004, a new highly pathogenic strain of avian influenza, H5N1, spread across Asia, infecting poultry and humans. Although the virus is incapable of sustained human-to-human transmission, the virus continues to mutate. According to the World Health Organization, as of March 5, 2008, 371 people had been infected with H5N1 virus across 14 countries, resulting in 235 deaths.

While the flu affects individuals of all ages, approximately 90% of flu-related deaths occur among individuals above the age of 65. People with chronic medical conditions and young children also have a higher risk of suffering influenza complications.

Geographical distribution

The influenza virus occurs worldwide. In temperate regions, influenza occurs during the winter months, affecting the northern hemisphere from November to March and the southern hemisphere from April to September. In tropical regions influenza may occur at any time of the year.

Transmission

Influenza transmission occurs mostly by breathing in respiratory droplets that enter the air when an infected person coughs or sneezes. Transmission also occurs through direct contact with respiratory droplets or secretions, followed by touching the nose or mouth.

Symptoms

Influenza leads to a variety of symptoms, ranging from mild to severe. Common symptoms include fever, headache, muscle ache, extreme fatigue, sore throat, cough and nasal congestion. While symptoms usually abate within one to two weeks, a common misconception about influenza is that the symptoms of stomach flu (vomiting, diarrhea, and nausea) are related to influenza. Stomach flu is commonly caused by bacteria or parasites and is rarely related to the influenza virus.