

## MF59<sup>®</sup> Adjuvant Fact Sheet

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### **MF59<sup>®</sup> Adjuvant**

MF59<sup>®</sup>, Novartis Vaccines' proprietary adjuvant, is the first oil-in-water adjuvant to be commercialized in combination with a seasonal influenza vaccine (Fluad<sup>®</sup>). Fluad is currently licensed for use in people 65 years of age and above. Designed to enhance the body's immune response to prepandemic, pandemic and seasonal influenza vaccines, MF59 increases the immune response compared to non-adjuvanted vaccines.

Novartis Vaccines  
proprietary adjuvant

MF59 has been tested extensively – in more than 60 clinical trials involving more than 33,000 people. With more than 12 years of clinical experience and more than 45 million doses of adjuvanted vaccines distributed, MF59 has an established safety profile and has been shown to be well tolerated in children, adults and the elderly.

Clinical trial results with  
MF59

Studies have shown that MF59 helps elicit broad, cross-reactive immune responses against a wide range of influenza strains, including some strains not contained in a seasonal influenza vaccine, as well as the majority of H5 avian influenza virus strains. The adjuvant has also demonstrated the ability to provide strong immune memory and sustained antibody responses when included in both seasonal and prepandemic vaccines. This response can help the immune system produce a protective response when boosted several years following initial vaccination.

MF59 helps elicit broad  
cross-reactive immune  
responses

Novartis Vaccines has utilized MF59 to develop influenza vaccines designed specifically for those who need it most – individuals who have compromised immune systems, such as young children and older adults, and people with no natural immunity to a virus. The first MF59-adjuvanted vaccine was Fluad, an inactivated, subunit seasonal influenza vaccine shown to provide a greater immune response than traditional inactivated influenza vaccines in individuals aged 65 years and older. First registered in Italy in 1997, Fluad marked a major milestone in influenza vaccinology.

MF59-adjuvanted vaccines

Currently, MF59 is being studied in Aflunov, an investigational prepandemic influenza vaccine adjuvanted with MF59. In clinical trials Aflunov has demonstrated a strong immune response against several H5N1 avian influenza virus strains in all age groups – from young children to older adults.

In response to the World Health Organization's declaration of the H1N1

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pandemic in June 2009, Novartis Vaccines also is studying MF59 in combination with two H1N1 pandemic vaccines: Focetria and Celtura. Focetria is a mock-up pandemic influenza vaccine that is indicated for use in the European Union during a pandemic situation. Celtura is a pandemic vaccine developed using cell culture technology. In September 2009, in its initial clinical trials, Celtura showed favorable results which suggested that one dose of the vaccine provided comparable protection to two doses of non-adjuvanted vaccines.

### **Adjuvants**

Adjuvants were originally identified in the 1920s by Gaston Ramon, a French veterinarian working at the Pasteur Institute in Paris. Ramon noticed that when he added certain substances to his vaccines, they generated a stronger immune response than ordinary formulations. Ramon named these substances “adjuvants” after *adjuvare*, the Latin word for “to help,” and they became an indispensable ingredient in vaccines against everything from hepatitis to meningitis to rabies.

Adjuvants first developed in 1920

The only problem, as Ramon quickly discovered, was that only salts of aluminum – collectively referred to as alum – seemed safe for human use, but alum does not always generate an optimal immune response. Despite intense efforts by vaccinologists to find more effective alternatives, a new, safe adjuvant was not discovered until Novartis Vaccines created MF59.

MF59 was developed in the 1990s by researchers at Ciba-Geigy (a Novartis heritage company) and Chiron (acquired by Novartis in 2006) who were searching for an adjuvant that was not only capable of improving the immune response but was also well tolerated. The resulting compound – subsequently named MF59 – demonstrated a good safety profile in people and was able to “jump start” the innate immune response, a vital part of the immune system that determines the magnitude and precise nature of the body’s immune response to an infection.

History of MF59

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Historically, vaccine development has focused on refining the antigen – proteins that stimulate the production of an antibody and provide the immune response. Increasingly, vaccines are made from purified antigens rather than inactivated – or killed – viruses. While this can produce better characterized antigens and help reduce potential reactions, purified antigens are less likely to spark an innate immune response; this issue necessitates the use of an adjuvant.

Novartis Vaccines researchers have made significant progress in unraveling how adjuvants fuel the immune response. Their research has revealed that adjuvants help increase antibody production by activating one or more components of the immune system, including:

- recruiting immune cells to the injection site, which increases the immune response to the influenza vaccine
- promoting the uptake of influenza vaccine antigens into immune cells, which boosts the immune response.

Because adjuvants bolster the body's immune response to a pathogen, a smaller amount of antigen is required to trigger protective immunity. Studies have shown that MF59 can reduce the amount of antigen required to generate an immune response for both seasonal and prepandemic vaccines.

How adjuvants work

### **Seasonal influenza**

Seasonal influenza is a highly communicable, acute viral infection that predominantly attacks the respiratory tract and sometimes the lungs. It can cause mild to severe illness and may lead to death. Between 5 and 15 percent of the worldwide population is infected each year and between 250,000 to 500,000 people die. More than 90 percent of deaths associated with influenza in industrialized countries occur among those 65 years of age and over.

Dangers of seasonal influenza

Despite the severity of the illness, many people mistakenly believe that influenza is merely a severe cold. While colds and influenza share many symptoms, they are caused by different viruses and result in different consequences for patients. Influenza-related complications can include pneumonia and dehydration, and worsening of chronic conditions, such as congestive heart failure, asthma, chronic obstructive pulmonary disease or diabetes.

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### **Pandemic influenza**

An influenza pandemic occurs when a new influenza strain, to which people have no immunity, emerges, mutates and spreads globally. Three influenza pandemics have occurred during the 20th Century. The deadliest was in 1918 and resulted in as many as 50 million deaths worldwide. The 1968 pandemic caused about 700,000 deaths around the world. During the last four centuries, an influenza pandemic has emerged about once every 30–40 years.

Pandemics take toll on worldwide population

H1N1 influenza – initially referred to as ‘swine flu’ - was first detected in April 2009 in Mexico and the U.S. Since then, the virus has spread rapidly from person to person around the world and has been identified in more than 70 countries. In June 2009, the World Health Organization (WHO) raised the pandemic alert level to Phase 6 in response to the ongoing global spread of the virus.

Influenza A(H1N1) “Swine flu”

Prior to the emergence of the H1N1 pandemic health authorities had identified H5N1 avian influenza as one of the influenza strains with pandemic potential. H5N1 is currently circulating in birds around the world, and has already shown it can transmit to people. H5N1 has a case fatality rate of almost 60 percent.

Influenza H5N1 “Bird flu”

### **Vaccination**

Vaccination is one of the most significant public health interventions ever implemented, sparing millions of people from suffering infectious diseases. Use of currently available influenza vaccines has been calculated to save more than 8 million lives annually, translating to one person saved every five seconds.

Importance of influenza vaccinations

When properly primed, the body is able to develop a protective immune response against an infection faster and help ward off serious flu-related complications.

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