The history, facts, and future of the most effective and revolutionary public health intervention

VACCINES

PROTECT YOUR HEALTH
AT EVERY AGE
A Legacy of Achievement in Preventing Disease

Pfizer has a long history of researching and developing vaccines. Our current research program includes innovative preventative and therapeutic vaccines.

Reference

- Wyeth
- Lederle Laboratories
- Praxis Biologics
- Lederle-Praxis Biologics
- Wyeth Lederle Vaccines and Pediatric
- Pfizer
- Pfizer, Pipeline as of November 2012. Available at http://www.pfizer.com/research/product_pipeline/product_pipeline.jsp
A Legacy of Achievement in Preventing Disease

Pfizer has a long history of researching and developing some of the world’s most important vaccines. Our current research program includes innovative preventative and therapeutic vaccines.

1988
First to license a conjugate-based vaccine for Haemophilus influenzae type b when HibTITER is licensed for toddlers in the United States.

1991
First to license a Haemophilus influenzae type b (Hib) vaccine combined with DTP in the United States.

1993
First to license a 7-valent pneumococcal conjugate vaccine [Diphtheria CRM197 Protein], for the prevention of invasive pneumococcal disease caused by vaccine serotypes in infants and toddlers.

1999
First to license a 13-valent pneumococcal conjugate vaccine, for use in adults 50 years and older.

2000
First to license a Haemophilus influenzae type b (Hib) vaccine combined with DTP in the United States.

2010
First to license a meningococcal serogroup C conjugate vaccine.

2011
Pfizer is currently investigating vaccines against Meningitis B (phase 3); Alzheimer’s disease (phase 2); Staphylococcus aureus (phase 2); Clostridium difficile colitis (phase 1) and smoking cessation (phase 1).

Pfizer has a long history of researching and developing some of the world’s most important vaccines. Our current research program includes innovative preventative and therapeutic vaccines.
Vaccination is the most effective and economical way of preventing infectious diseases. Vaccines have led to the control, lower incidence and even elimination of diseases in Europe that in the past resulted in death or disability for millions of people.2

– Council of the European Union,
6 June 2011

Table of Contents

• What is a Vaccine? 5
  – The Vaccine Revolution 5
  – Life-Saving Prevention 6
  – Making Vaccines: Science at Its Best 7
• Vaccines: The Key to Protecting Health at Every Age 9
  – Adult Vaccination Rates – Why So Low? 9
  – As We Get Older, Health Means Wealth 10
• Why Do So Many Myths Persist? 11
  – The High Price of Non-Vaccination 12
  – Helping Curb Bacterial Multi-Drug Resistance 12
  – A Call for Better Public Defense of Vaccines 12
• The Future of Vaccines 13
• Pfizer’s Commitment to Global Health 14
• Appendix 15
  – Key Dates in Vaccines History 15
  – Terms and Definitions 18
• References 21
What is a Vaccine?

A vaccine is a biological preparation which usually contains a severely attenuated, weakened or inactivate version of the virus or bacteria (also called “pathogen”) that it is meant to prevent. Introducing this biological preparation into the body prompts the immune system to combat the specific although inactive pathogen, and thus prepares the body to fight it in the future by creating an “immune memory.” As a result, a vaccinated person has the tools needed to recognize and effectively fight off a “live” version of the pathogen and prevent a potentially deadly infection.3

The Vaccine Revolution

The world’s first vaccination was performed by Edward Jenner in 1796 against smallpox. A century later, Louis Pasteur developed the first rabies vaccine. Since then, scientific research and progress has led to the development of over 30 vaccines against some of the most deadly diseases known to man such as typhoid, polio, and measles.5 Thanks to effective routine childhood immunisation, diseases with serious outcomes such as polio, diphtheria or tetanus are now almost eradicated from the European Union.6

“Vaccines have changed the face of medicine in just 200 years. Along with improvements in sanitation and clean water, vaccination is now recognized as the most successful & effective public health intervention in the world for saving lives and promoting good health.”

– WHO & UNICEF
**Life-Saving Prevention**

Vaccines are an essential component of disease prevention. They are responsible for the global eradication of smallpox as well as saving over 3 million lives worldwide each year, and millions more from suffering illness and lifelong disability. Vaccines enable people to lead longer, healthier lives and also help reduce health care costs to both individuals and the broader health care system by reducing the incidence of vaccine-preventable illness. In addition, vaccines help protect society’s most vulnerable members — including infants, the elderly and groups at risk — from deadly diseases such as meningitis, pneumonia and measles.

However there is a continuing need to develop vaccines that better address the needs of specific populations, such as those with weakened immune systems, for whom current vaccine options may not be suitable.

**Vaccines have eradicated some of the world’s deadliest diseases**

Comparison of 20th Century Annual Morbidity** and Current Morbidity: Vaccine-Preventable Diseases8

<table>
<thead>
<tr>
<th>Disease</th>
<th>20th Century Annual Rate of New Cases†</th>
<th>2010 Reported Cases††</th>
<th>Percent Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smallpox</td>
<td>29,005</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>21,053</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Measles</td>
<td>530,217</td>
<td>61</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Mumps</td>
<td>162,344</td>
<td>2,528</td>
<td>98%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>200,752</td>
<td>21,291</td>
<td>89%</td>
</tr>
<tr>
<td>Polio (Paralytic)</td>
<td>16,316</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Rubella</td>
<td>47,745</td>
<td>6</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Congenital Rubella Syndrome</td>
<td>152</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Tetanus</td>
<td>580</td>
<td>8</td>
<td>99%</td>
</tr>
<tr>
<td>Haemophilus Influenzae</td>
<td>20,000</td>
<td>270*</td>
<td>99%</td>
</tr>
</tbody>
</table>

†† Source: CDC. MMWR January 7, 2011: 59 (52): 1704–1716. (Provisional MMWR week 52 data)
** Morbidity means annual rate of new cases
†6 type b and 254 unknown serotype (<5 years of age)

Comparison of Pre-vaccine Era Estimated Annual Morbidity or Mortality with Current Estimate: Vaccine-preventable Diseases8

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pre-vaccine Era Annual Estimate</th>
<th>2008 Estimate</th>
<th>Percent Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A</td>
<td>117,333†</td>
<td>11,049</td>
<td>91%</td>
</tr>
<tr>
<td>Hepatitis B (Acute)</td>
<td>66,232†</td>
<td>11,269</td>
<td>83%</td>
</tr>
<tr>
<td>Pneumococcus (Invasive) all ages</td>
<td>63,067†</td>
<td>44,000#</td>
<td>30%</td>
</tr>
<tr>
<td>&lt;5 years of age</td>
<td>16,069†</td>
<td>4,167##</td>
<td>74%</td>
</tr>
<tr>
<td>Rotavirus (Hospitalizations, &lt;5 years of age)</td>
<td>62,500**</td>
<td>7,500###</td>
<td>88%</td>
</tr>
<tr>
<td>Varicella</td>
<td>4,085,120†</td>
<td>449,363</td>
<td>89%</td>
</tr>
</tbody>
</table>

† Source: JAMA. 2007; 298 (18): 2155–2163
†† Source: CDC. MMWR. February 6, 2009 / 58 (RR02): 1–25
### Source: New Vaccine surveillance Network
Making Vaccines: Science at Its Best

Manufacturing vaccines is a complex and highly technical process that involves stringent quality and safety procedures. Vaccines are biological products which are very sensitive to change and are highly controlled throughout the manufacturing process.9

The first step in manufacturing a vaccine is to produce the active component of the vaccine, which is usually a severely attenuated, weakened or inactivated version of the virus or bacteria, rendering it safe to administer to individuals. Manufacturing processes are then vaccine-specific.

Conjugate Technology

In the case of Pfizer’s 13 valent pneumococcal vaccine, thirteen polysaccharides molecules are manufactured and then bonded or conjugated with a carrier protein that helps to elicit an immune response in the immune system. The process of conjugating 13 serotypes is considerably complex as each serotype must be made separately in precise quantities to achieve the correct clinical immunological response.

• Typically it takes around a year to complete the full cycle of production and testing stages for each batch of Pfizer’s 13 valent pneumococcal vaccine.
• Over 300 separate quality controls tests are conducted during the production of each batch of vaccine, to help ensure that Pfizer’s 13 valent pneumococcal vaccine meets the requirements for purity, potency and safety.
• Scientists perform between 10,000 to 15,000 tests per month on the manufacturing environment the vaccines are being made.

“Vaccines are without questions held to the single highest standard of safety than any other biological or drug.”

Prof. Dr. Heinz-J. SCHMITT, FIDSA, Senior Director Scientific Affairs (Vaccines) Europe, Pfizer
Pfizer’s Grange Castle Biotechnology Campus is one of the largest biotech manufacturing sites in the world. Pfizer recently invested $200 million in the site to introduce two new processing suites and expand current production and product testing capabilities for a number of products including Pfizer’s 13 valent pneumococcal conjugate vaccine.10

**The stages in the manufacturing process**

**Activation of the Serotypes**
The active components of each of the 13 vaccines contained in Pfizer’s 13 valent pneumococcal vaccine are the polysaccharides or large sugar polymers on the surface of the pathogenic bacterium, Streptococcus pneumoniae. The first step of the process involves the fermentation or growth of the organism in large tanks followed by the purification of the polysaccharide.

**Vaccine Conjugation**
The polysaccharide is then chemically bound or conjugated to a special carrier protein to form a glycoconjugate, and the glycoconjugate is then purified to a pure substance. Thirteen different glycoconjugates are manufactured for Pfizer’s 13 valent pneumococcal vaccine.

**Ultrafiltration and Fill**
After conjugation, a number of ultrafiltration steps are carried out for purity and concentration of the product before being filled. At the filling stage, the product is transferred to individual bags of conjugate. Each conjugate bag will only hold one serotype. Next, each of the 13 separate conjugates that represent the 13 serotypes found in Pfizer’s 13 valent pneumococcal vaccine is combined to create the vaccine in bulk liquid form in a process called formulation.

**Syringe Filling**
After passing extensive quality control tests on a manufacturing line, Pfizer’s 13 valent pneumococcal conjugate vaccine is dispensed into syringes, in preparation for final packing labelling and distribution. Additional quality tests are conducted on the finished product.
Vaccines: The Key to Protecting Your Health at Every Age

Amongst adults, vaccine-preventable diseases remain a significant threat. A 2009 study reported that in the USA, significantly more adults than children die from vaccine-preventable diseases, such as influenza, pneumococcal disease, tetanus, diphtheria, pertussis (whooping cough), each year. In Europe, both the burden of vaccines-preventable diseases and vaccination rates amongst older adults are under-monitored. When data is available, it points to sub-optimal levels of vaccination rates.

Adult Vaccination Rates – Why So Low?

- **FLU**: In Europe, most countries do not reach the targeted rate of 75% vaccination rates for flu – the most well known and recognized vaccine – for older adults.
- **PNEUMOCOCCAL DISEASES**: Immunisation rates for pneumococcal diseases amongst older adults have been low, ranging between 20% and 30%. The UK has had the highest cumulative coverage rate (over 69%), where active campaigns to promote pneumococcal vaccination for elderly adults and younger persons at risk began in 2003.

“Adults were shown to be 100 times more likely to die from vaccine-preventable diseases than children in the USA.” – American College of Physicians

In Europe, vaccines coverage in adults for a variety of serious vaccine-preventable diseases remains low and unpredictable while the burden remains high amongst older adults.
These low and inconsistent rates of vaccination among adults have complex root causes but can be partially explained by the misplaced belief that vaccination is only for the young on the one hand, and the reliance on risk-based guidelines for adults on the other. Contrary to vaccination guidelines for young children where specific recommendations are established from birth to age five, adult vaccination recommendations tend to be patchy and focused on the existence of other diseases, such as asthma, HIV, or other diseases that affect an individual’s ability to fight off vaccines-preventable diseases.

There is a growing interest and discussion around establishing European best-practice guidelines which would mimic the model and hence the effectiveness of childhood immunisation schedules. Such “age-based” guidelines would be more easily understood by both practitioners and patients, and would be easier to implement than a multitude of risk-based guidelines which require identifying individuals with specific diseases and usually fail to achieve high coverage levels.

**As We Get Older, Health Means Wealth**

Currently four people of working age support one “retiree”. By 2050, this ratio will drop to two for every retired person. The European Commission estimates that member states health care spending will increase by approximately 25% (gross domestic product) in most Member States due to the growing number of older citizens alone. As governments push back retirement ages to meet this future challenge, prevention strategies such as adult vaccination programs have the potential to keep Europe’s senior population active and healthy.

Europe’s population is ageing fast and has the highest proportion of “older people (60+)” of all continents. – UN

---

**figure 2:** The burden of pneumococcal disease amongst older adults: Notification rates for invasive pneumococcal disease by age and sex in 17 European countries in 2008 (n=12,427)

**figure 3:** Population distribution in EU25 by age group (1950-2050).
Why Do So Many Myths Persist?

Despite the success of childhood immunisation programs, and undisputable evidence that vaccines are safe and effective, false and misleading information continues to circulate regarding vaccines in general. This misinformation leads people to question the value of vaccines, resulting in a drop in vaccination rates and new outbreaks of old diseases. Both the European Centre for Disease Prevention & Control (ECDC) and the World Health Organization (WHO) have called on all stakeholders to partner together to counter common myths and inaccuracies.20

<table>
<thead>
<tr>
<th>MYTHS</th>
<th>FACTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>“People who get vaccinated for the flu often wind up getting it.”</td>
<td>• This is false. Certain vaccines can lead to mild symptoms resembling the disease against which they provide protection, but those are mainly a consequence of the immune system gearing up to produce the immune response.21</td>
</tr>
<tr>
<td>“Vaccines cause side effects, illnesses, and even death – not to mention possible long-term effects we don’t even know about.”</td>
<td>• The vast majority of side effects are minor and temporary, such as a sore arm or mild fever, and have nothing to do with the infectious disease against which the immunisation is directed.22 New vaccines go through a rigorous testing in development and approval phases in Europe, to make sure they are safe, effective and of good quality.23 The European Medicines Agency also monitors any adverse events that might occur after licensure of the medicine.</td>
</tr>
<tr>
<td>“Vaccine-preventable diseases have been virtually eliminated from Europe, so there is no need for my child or myself to be vaccinated.”</td>
<td>• This is one of the most damaging myths today. Past vaccination programs do not eliminate the need for adults, young people and children to be vaccinated today. The indirect protection against disease (also called “herd immunity”), only results when a sufficient number (from 85% to 95% depending on the disease24) of individuals in a community are immune to that disease. For example, diphtheria requires 85 percent of the population to be vaccinated, while measles and mumps immunization levels must approximate 92–96% and 88–92% respectively before herd immunity becomes effective.25</td>
</tr>
</tbody>
</table>

“Routine childhood vaccines effectively protect between 85% and 95% of recipients against the targeted diseases.”24

– Fine & Mulholland
The High Price of Non-Vaccination

Unfortunately, all of these misperceptions have led some individuals to avoid vaccinations for either themselves or their family members, and the cost to individuals and society is measurable and high.

- **New outbreaks of old diseases**
  While most vaccines-preventable diseases’ prevalence is being kept at very low levels, recent outbreaks of measles, and even poliomyelitis, across Europe attest to the fact that these diseases still pose a threat if vaccination coverage is not kept high.26

- **High cost of hospital stays and lost days of work**
  The annual cost-burden for treating pneumonia alone across Europe is 10 billion Euros mostly due to in-hospital care and lost work days.27

**Helping curb bacterial multi-drug resistance**

While some vaccine-preventable diseases can be treated with antibiotics, over-utilisation of antibiotics leads to drug resistance, which increases the risk of infectious disease outbreaks and the potential for widespread illness.29 Since the mid-1990s the proportion of pneumococci bacteria resistant to antibiotics has increased in many European countries from a few percent to 5–35%.30

These cases are estimated to result in extra healthcare costs and productivity losses of at least EUR 1.5 billion each year, a burden likely to increase as numbers rise.31

Encouraging vaccination along with more appropriate use of antibiotics can lower drug resistance rates by reducing the ability of infectious agents to develop resistance mechanisms.

A Call For Better Public Defense Of Vaccines

Healthcare professionals and public health officials are equally concerned with the rise of antibiotic-resistant bacteria and the dwindling number of antibiotics that remain to treat infections. Vaccines information should be part of the development of a European public health communication strategy that allows European citizens to better understand the value of vaccines, assess their individual risk in relation to vaccines-preventable illness and manage their own health.

“ In 2008, 90% of the people who contracted measles in EU/EEA countries had not been immunised.28”

– ECDC
The Future of Vaccines

Future vaccines will not only prevent infectious diseases, but research is also on-going into “therapeutic” vaccines to cure such chronic diseases as diabetes, Alzheimer’s and nicotine dependence. It’s expected that vaccines will go beyond their traditional prevention remit to treat autoimmune diseases and allergic disorders. In addition, work is also underway to develop new ways of administering vaccines like transcutaneous\(^\text{A}\) and orally. Those medical and technological advances are void if not coupled with comprehensive programs to ensure full understanding of the benefits and safety of vaccines, as well as life-course vaccination guidelines to ensure wide and timely access to these vaccines.

“\text{The first decade of this century has been the most productive in the history of vaccine development.}^{32}\text{ – WHO}”

200 candidates in development\(^33\)

- Clostridium difficile
- Cytomegalovirus virus
- Dengue fever
- Ebola virus
- Enterotoxigenic Escherichia coli
- Herpes simplex
- HIV
- Malaria
- Meningococcal B disease
- SARS
- Staphylococcus aureus
- Tuberculosis
- Addiction (Cocaine, Nicotine)
- Allergies
- Alzheimer’s
- Cancer
- Multiple sclerosis
- Parkinsons

\(^{\text{A}}\text{ Delivery of vaccine to the skin, via patches for instance.}\)
Pfizer’s Commitment to Global Health

Pneumococcal diseases overwhelmingly burdens young children and the elderly, and kill over 1.6 million people each year – including approximately 800,000 children before their 5th birthday. More than 90% of these deaths occur in developing countries. Through the Advanced Market Commitment (AMC) program, Pfizer reaffirmed its commitment to working with the global health community to accelerate global access to its vaccines in the world’s poorest countries on an affordable and sustainable basis.

As of December 2011, Pfizer’s 13 valent pneumococcal conjugate vaccines is available in more than 85 percent of countries which have launched pneumococcal immunisation programs under the AMC with many additional launches planned.

To meet the growing global demand, Pfizer is investing resources to increase its manufacturing capabilities and in the development of a preserved, multidose vial which, subject to WHO prequalification, is expected to offer an alternative option for developing countries.

For more information on the GAVI Alliance, visit: http://www.gavialliance.org/

For more information on Pfizer’s vaccines activities, visit: www.pfizer.com


"Pfizer has pledged to supply up to 480 million doses of its 13-valent pneumococcal conjugate vaccine through 2023 in developing countries, under the auspices of the Advance Market Commitment (AMC), an innovative program piloted by the GAVI Alliance to enable affordable access to medicines by developing countries."
### Scientific History of Vaccines

**Introduction of Vaccines: historical time-line (1796-2004)**

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>429 BC</td>
<td>Thucydides notices that smallpox survivors do not get re-infected.40</td>
</tr>
<tr>
<td>900 AD</td>
<td>Chinese discover variolation—a primitive form of vaccination aimed at preventing smallpox by exposing healthy people to tissue from the scabs caused by the disease.40</td>
</tr>
<tr>
<td>1796</td>
<td>Smallpox (live-attenuated) Dr Edward Jenner, British physician, discovers vaccination40. The first smallpox vaccination is created. Vaccination became popular throughout Europe and, soon after, the US41.</td>
</tr>
<tr>
<td>1885</td>
<td>Rabies (killed-inactivated)* Cholera (killed-inactivated)* Typhoid (killed-inactivated)* Diphtheria (D) (toxoid) Pertussis (Pw), whole cell (killed-inactivated) Tetanus (T) (toxoid) Tuberculosis (BCG) (live-attenuated).</td>
</tr>
<tr>
<td>1928</td>
<td>Yellow fever (live-attenuated)</td>
</tr>
<tr>
<td>1936</td>
<td>Influenza (killed-inactivated)*</td>
</tr>
<tr>
<td>1937</td>
<td>Tickborne encephalitis (killed-inactivated)*</td>
</tr>
<tr>
<td>1945</td>
<td>Japanese B encephalitis (killed-inactivated)</td>
</tr>
<tr>
<td>1955</td>
<td>Polio (IPV) (killed-inactivated) DTPw</td>
</tr>
<tr>
<td>1958</td>
<td>Polio (OPV), oral polio vaccine (live-attenuated)</td>
</tr>
<tr>
<td>1961</td>
<td>DT-IPV</td>
</tr>
<tr>
<td>1963</td>
<td>Measles (M) (live-attenuated)</td>
</tr>
<tr>
<td>1966</td>
<td>DTPw-IPV</td>
</tr>
</tbody>
</table>

Replaced by a new vaccine
1. Pneumococcal disease (23 serotypes – polysaccharide)
2. Varicella-zoster (live-attenuated)
3. HB (protein/recombinant DNA)
4. Influenza (subunit)
5. Haemophilus influenzae type b (Hib) (polysaccharide-protein conjugate)

Typhoid (live-attenuated)*
Hepatitis B (HB) (protein)
Pertussis acellular (Pa)

1981

Influenza (subunit, adjuvanted)

1983

DTPa
Meningococcal disease (serogroup C – polysaccharide-protein conjugate)

1997

HA-Typhoid (polysaccharide)
dTaP-IPV
DTPa-IPV-HB
Pneumococcal disease (7 serotypes – polysaccharide-protein conjugate)

1999

Pseudomonal disease (8 serotypes – polysaccharide)

2000

Influenza (live-attenuated)
Meningococcal disease (serogroups ACW – polysaccharide)

2001

DTPa-Hib
DTPa-IPV-Hib

2003

Pneumococcal conjugate vaccine, 13-valent, licensed in Europe for adults 50+.

2006

HPV vaccine approved in Europe.

2009

Pandemic Influenza vaccine approved in Europe.

2009

Pneumococcal conjugate vaccine, 13-valent, licensed in Europe for infants and young children.

2011

Pneumococcal conjugate vaccine, 13-valent, licensed in Europe for adults 50+. 
Epidemiological, social & political history of Vaccines

1700s
Variola spreads around the world. At this time, smallpox was the most infectious disease in Europe, killing up to one-fifth of those infected in numerous epidemics. Variola caused mild illness but, although it occasionally caused death, smallpox rates were lower in populations that tried it.40

1870s
Violent opposition to vaccination. People found it hard to believe that it really worked. They also felt that it took away people’s civil liberties, particularly now that it was compulsory.40

1956
WHO launches global drive to eradicate smallpox.40

1974
Launch of the World Health Organization’s Expanded Program on Immunisation (EPI), including six vaccines, covering diphtheria, tetanus, whooping cough, measles, polio, and tuberculosis. Before 1974, only 5 per cent of children were vaccinated against these diseases. Today over 70 per cent are vaccinated.43

1980
Smallpox eradicated from the world.40

1988
WHO launches global drive to eradicate polio by the year 2000.41

1999
WHO set up a Global Advisory Committee on Vaccine Safety, made up of independent experts, to respond promptly, efficiently, and with scientific rigour, to rumours and reports related to vaccine safety.44

2000
Global Alliance for Vaccines and Immunisation established to strengthen routine vaccinations and introduce new and under-used vaccines in countries with a per capita GDP of under US$1000. GAVI is now entering its second phase of funding, which extends through 2014.

Sep. 2010-2011

Sep. 2010
Measles outbreak in Europe.65

2010
Reemerging cases of Polio in Europe.67

2010
Member States in the WHO European Region set themselves 2015 as new target for eliminating measles and rubella.66
Terms and Definitions

**Adjuvants:** A substance (e.g. aluminum salt) that is added during production of a vaccine to increase the body’s immune response to a vaccine.48

**Antibody:** A protein found in the blood that is produced in response to a foreign substance (e.g., bacteria or viruses) invading the body. Antibodies protect the body from disease by binding to these organisms and destroying them.48

**Antigens:** Foreign substances (e.g., bacteria or viruses) in the body that are capable of causing disease. The presence of antigens in the body triggers an immune response, usually the production of antibodies.48

**Attenuated Vaccine:** A vaccine created by reducing the virulence of a pathogen but still keeping it ‘live’ so as to ensure an immune response. The aim is to render the living agent harmless or less virulent.49

**Conjugate vaccine:** A vaccine in which two compounds (usually a protein and polysaccharide) are joined together to increase a vaccine’s effectiveness. Conjugate vaccines include certain pneumococcal and meningococcal vaccines.50

**Herd immunity:** Indirect protection against disease that results from a sufficient number (from 85 to 95% depending on the disease26) of individuals in a community having immunity to that disease. Herd immunity does not apply to diseases such as tetanus, that are not spread via person-to-person contact.51

**Immunogen:** A substance able to provoke an immune response. “Immunogenicity” refers to an immunogen’s ability to provoke such a response under particular circumstances.51

**Immunotherapeutic vaccines:** vaccines designed to treat against conditions beyond the infectious diseases or cancer arena. Most of the candidates are still in early-stage development and their underlying scientific bases require additional investigation: Smoking cessation52, Alzheimer’s disease; Allergies; Diabetes; Atherosclerosis Hypertension53; Multiple Sclerosis.

**Inactivated vaccine:** A type of vaccine in which the vaccine pathogen (a viral or bacterial) is killed or otherwise altered so that it cannot cause infection, but can still provoke an immune response.51

**Pathogen:** A microorganism capable of producing a disease (e.g., bacterium or virus).54

**Prophylactic vaccine:** A biological preparation intended to prevent individuals from contracting given diseases.

**Therapeutic vaccines:** vaccines which intend to treat chronic infections by inducing immune responses that suppress infection, even when the host has been unable to create those responses naturally.52

**Selected vaccines-preventable diseases:**

**Diphtheria**
Diphtheria is an acute disease caused by toxin-producing strains of Corynebacterium diphtheriae bacteria, that is known to colonise mucous membranes.55 Diphtheria affects people of all ages, but most often it strikes unimmunized children. In 2,000, 30,000 cases and 3,000 deaths of diphtheria were reported worldwide.56

**Haemophilus influenzae type b infection**
*Haemophilus influenzae* serotype b (Hib) is the most common cause of bacterial meningitis in children aged two months to five years, in those countries where suitable vaccination programmes are not in place.55 Hib is estimated to cause millions of cases of serious disease worldwide and hundreds of thousands of deaths each year among young children.57

**Hepatitis A:** Hepatitis A is a liver disease caused by the hepatitis A virus (HAV). Hepatitis A can affect anyone.58

**Hepatitis B:** is a serious disease caused by a virus that attacks the liver. The virus, which
is called hepatitis B virus (HBV), can cause lifelong infection, cirrhosis (scarring) of the liver, liver cancer, liver failure, and death.\textsuperscript{59}

**human papillomavirus (HPV)**, HPV is a common infection: over three quarters of sexually active women are estimated to be infected at least once in their lifetimes. Persistent infection with oncogenic HPV types can cause cervical cancer in women and anogenital cancers in both sexes.\textsuperscript{60}

**Influenza (seasonal)**: Influenza (the flu) is a contagious respiratory illness caused by influenza viruses. It can cause mild to severe illness, and at times can lead to death. Some people, such as older people, young children, and people with certain health conditions, are at high risk for serious flu complications.\textsuperscript{61}

**Measles**: Measles is highly infectious vaccine-preventable disease caused by morbillivirus. The disease is transmitted via airborne respiratory droplets, or by direct contact with nasal and throat secretions of infected individuals.\textsuperscript{55} Measles is one of the leading causes of childhood mortality, leading to about 240,000 deaths worldwide each year.\textsuperscript{62}

**Meningococcal infection**: Meningococcal infection is caused by *Neisseria meningitidis*, a bacterium with human carriers as the only reservoir.\textsuperscript{55} Meningococcal group C (or Meningitis C) is one of the 6 groups of the bacteria *Neisseria meningitides* which can cause meningitis and septicaemia.

**Mumps**: Mumps is an acute illness caused by the mumps virus. It is characterised by fever and swelling of one or more salivary glands.\textsuperscript{55} Mumps is mostly a mild childhood disease. It most often affects children between five and nine years old.\textsuperscript{63}

**Pertussis**: Pertussis is an acute bacterial infection of the respiratory tract caused by the bacterium Bordetella pertussis. The disease is characterised by a severe cough.\textsuperscript{55} Pertussis (whooping cough) is an important cause of infant death worldwide and continues to be a public health concern even in countries with high vaccination coverage. Estimates from WHO suggest that, in 2008, about 16 million cases of pertussis occurred worldwide, 95% of which were in developing countries, and that about 195,000 children died from the disease.\textsuperscript{64}

**Pneumococcal infection**: [Pneumococcal Disease (PD) describes a group of illnesses caused by the bacterium Streptococcus pneumoniae (*S. pneumoniae*), also called pneumococcus, and can include invasive infections such as meningitis, bacteremic pneumonia as well as noninvasive infections such as non-bacteremic pneumonia and acute otitis media.\textsuperscript{65} According to a WHO 2004 estimate, PD is the leading cause of vaccine-preventable death in children younger than 5 years of age worldwide.\textsuperscript{66} The proliferation of resistant strains of *S. pneumoniae* and other pathogens in the past 15 years threatens the successful treatment of CAP\textsuperscript{67} Pneumococcus vaccine is deemed underused by the WHO-Europe Office.\textsuperscript{68}

**Poliomyelitis**: Polio is caused by polioviruses, classified into types 1, 2 and 3. Humans are the only reservoir of infection. Transmission occurs via the oral-faecal route or contact with saliva.\textsuperscript{55} Polio is a highly infectious and sometimes fatal disease, which invades the nervous system and can cause paralysis in a matter of hours. The disease usually affects children under 5 years of age. In June 2002, all 53 countries in the WHO European Region were certified polio free. Since then, the region has experienced several episodes of wild poliovirus importation but sustained effort of immunisation and disease surveillance helps maintain the Region’s polio-free status.\textsuperscript{69}

**Rubella**: Rubella is a mild febrile rash illness caused by rubella virus. It is transmitted from person to person via droplets (the virus is present in throat secretions). It affects mainly, but not only, children and can often lead to serious and sometimes fatal complications in the fetus when an unprotected woman acquires the infection early in pregnancy. Humans are the only reservoir of infection.\textsuperscript{55}

**Rotavirus**: Rotavirus infection affects nearly all the children of the world. It causes about 25% of all diarrhoeal illnesses in children under 5, and is a major cause of morbidity and mortality globally. According to WHO estimates, more than 10,000 children under
5 die each year in the WHO European Region due to rotavirus infection. WHO/Europe works with Member States to accelerate the introduction of rotavirus vaccine into their national immunisation programmes, and to establish a regional surveillance network to collect local data on disease burden and monitor the impact of vaccines.70

**Shingles (Herpes Zoster):** Shingles is a painful localized skin rash often with blisters that is caused by the varicella zoster virus (VZV), the same virus that causes chickenpox. Shingles most commonly occurs in people 50 years old or older, people who have medical conditions that keep the immune system from working properly, or people who receive immunosuppressive drugs.71

**Smallpox:** Smallpox is a serious, contagious, and sometimes fatal infectious disease caused by the variola virus and characterized by extensive rash and higher fever.72 The global eradication of smallpox was certified in 1980.73

**Tetanus:** Tetanus is an often fatal disease, which is present worldwide, and affects people of all ages but is particularly common and serious in newborn babies. It is a consequence of a toxin produced by the bacterium Clostridium tetani. The main reservoirs of the bacterium are herbivores, which harbour the bacteria in their bowels (with no consequences for them) and disseminate the “spore form” of the bacteria in the environment with their faeces.55 WHO estimated that neonatal tetanus killed about 180,000 babies in 2002.74

**Varicella infection (chickenpox):** Chickenpox is caused by the varicella-zoster virus (VZV), which also causes shingles. The virus spreads through the body into the skin causing rashes to appear.55

**Yellow Fever:** Yellow fever is caused by the yellow fever virus, which is carried by mosquitoes. It is endemic in 33 countries in Africa and 11 countries in South America.75

**Other diseases against which Pfizer is investigating vaccines:**

**Alzheimer’s disease:** a degenerative disease, which slowly and progressively destroys brain cells, affecting memory and mental functioning.76 In 2010, 9.95 million individuals were suffering from Alzheimer in Europe and 35.6 million people worldwide.77 Predictions show the number will double over the next 20 years.78 Alzheimer also has an economic cost for society, which has been estimated at US$604 billion worldwide in 2010, comprising the cost of informal care, direct cost of social care, and the direct cost of medical care.79 This huge burden of disease is yet unaddressed as neither a preventative nor a curative treatment exist to date. Pfizer is currently investigating a vaccine in phase 2.80

**Staphylococcus aureus:** Staphylococcus aureus is an opportunistic bacterial pathogen associated with asymptomatic colonization of the skin and mucosal surfaces of normal humans. It is the most frequently isolated bacterial pathogen from patients with hospital-acquired infections. Before the introduction of antimicrobials in the 1940s, the mortality rate of S. aureus invasive infection was about 90%. The initial success of antibiotic therapy was rapidly countered by the successive emergence of penicillin-resistant, then methicillin-resistant S. aureus (MRSA) strains, and since 2002 by that of vancomycin-resistant strains.81 Pfizer is currently investigating a vaccine in phase 2.

**Meningitis B:** Meningitis is an infection of the meninges, the thin lining that surrounds the brain and spinal cord, caused by the bacteria *Neisseria meningitidis* group B, one of 6 groups of bacteria which cause disease.82 Serogroup B accounts for up to 80% of meningococcal disease in European countries such as UK, Norway, The Netherlands, Germany and Denmark.83 Pfizer is currently investigating a vaccine in phase 3.80

**Clostridium difficile colitis:** is a bacterium that causes inflammation of the colon, known as colitis. People who have other illnesses or conditions requiring prolonged use of antibiotics, and the elderly, are at greater risk of acquiring this disease. The bacteria are shed through feces.84 Pfizer is currently investigating a vaccine in phase 1.80

**Smoking Cessation:** Pfizer is currently investigating a vaccine for smoking cessation in phase 1.80
83. CDC. Meningitis in Other Countries webpage. Available at http://www.cdc.gov/meningitis/global.html.