



Vaccinations against
COVID-19. Innovative
technologies and efficiency.

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Warsaw, December 21, 2020

Version 1.0

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Introduction

Ladies and gentlemen,

the global COVID-19 pandemic, caused by the spread of the SARS-CoV-2 virus, has forced us to make changes in virtually every area of everyday life, from work or study to spending free time and family life. Many people have died in the wake of this pandemic, as a result of contracting COVID-19 or due to overloading health systems.

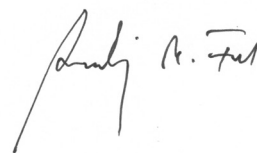
Today, thanks to the advent of vaccination, we have a chance to gain control of the SARS-CoV-2 virus and gradually return to the way of life before the pandemic. However, the positive effects depend largely on the mass vaccination coverage – the achievement of the appropriate level of immunization of the general public – and therefore on the common sense, knowledge, and decisions of each of us.

In the history of medicine development, immunization is one of the most outstanding achievements, a discovery that saved millions of people's lives. This contributed to the eradication of fatal and disabling diseases. Public health, understood as a holistic approach to medicine and healthcare in the fight against infectious diseases, has never had a more effective weapon.

Many Poles are extremely skeptical, even hostile, about vaccinations. The scientific community is aware that only overcoming social fears and actions based on substantive, reliable, and proven knowledge can change Poles' attitudes towards vaccination and thus contribute to high vaccination coverage and stopping the pandemic. That is why I invited a group of over a dozen renowned experts in various fields for years working for public health: infectious diseases, vaccinology, virology, chemistry and biochemistry, family medicine, to unite in the initiative 'Science Against the Pandemic' and to prepare a white paper entitled 'Vaccinations against COVID-19. Innovative Technologies and Efficiency' which is a compendium of knowledge about vaccination, its technology, and validity in fighting the pandemic.

The contents contained in the book support the medical community and medical services who have daily contact with patients and are usually the first source of knowledge for them. It is also a source of knowledge for the media and the general public, all who need science-based knowledge about vaccination against COVID-19, types of vaccines, and how they work.

In an era of overwhelmingly contradictory or unreliable information, as a group of authors, we hope that the white paper will clear up at least some of the doubts about the global COVID-19 pandemic, especially regarding the technology of mRNA vaccination, which is intensely developed in relation to this disease, and which is currently the only significant weapon we have in the fight against SARS-CoV-2.



Summary

Coronaviruses are a large family of RNA viruses that include species that infect humans and animals. In the 1960s, it was discovered that certain species of animal coronaviruses could also infect humans. In 2019, another animal coronavirus (later named SARS-CoV-2) became able to transmit and spread in humans, and the first outbreaks of COVID-19 appeared in China. On March 11, 2020, the WHO announced a pandemic, the epicenter of which quickly moved from Asia to Europe and North America. In Poland, at the beginning of December 2020, the total number of identified COVID-19 cases exceeded one million. COVID-19 can be life-threatening, especially among high-risk groups, and the epidemic spread of the disease, with such a high proportion of patients requiring hospitalization, rapidly overburdens the healthcare system.

Unfortunately, contracting COVID-19 does not equal the development of permanent immunity to the disease. So, we are faced with the simple choice of getting vaccinated against COVID-19 or taking part in the hard to predict lottery related to the disease and further deepening the health and economic crisis. However, the scale of the COVID-19 pandemic and the ease of human movement mean that only global action, including mass vaccination, will disrupt the virus's circulation. Vaccinations are the safest way to acquire immunity against COVID-19. In the case of SARS-CoV-2 vaccines, mRNA vaccines are currently under development. Research on this technology has been carried out for about 20 years, and it has great potential not only for the development of vaccines but also for the treatment of, e.g., cancer. mRNA vaccines are considered to be very safe due to the lack of the possibility of modifying the patient's DNA, the lack of the possibility of infection, the rapid degradation of the vaccine mRNA into harmless components and its similarity to the mRNA naturally occurring in cells, and a very small dose necessary to produce a therapeutic effect. Importantly, high titers of SARS-CoV-2 neutralizing antibodies were obtained seven days after the second vaccination in 90% of people. It is also worth noting that vaccines against COVID-19, like other vaccines available on the EU pharmaceutical market, undergo rigorous clinical trials and marketing authorization pro-

cedures. After COVID-19 vaccines are approved for use on the market, their safety will continue to be closely monitored according to legal standards. Moreover, their conditional approval, valid for one year, means that the European Medicines Agency will soon have to analyze the data on using these vaccines in clinical practice.

Logistics plays an essential role in an enterprise on such a scale as the distribution of COVID-19 vaccines. That is why the European Commission has issued a communication to the Member States recommending what a common vaccination strategy should look like, especially concerning vaccine distribution. On December 8, 2020, the National Immunization Program was adopted, taking into account the European Commission's above recommendations. Due to the massiveness, manufacturing procedure, and distribution of vaccines, the vaccination action will be phased. The order of priority groups, according to which vaccination will be carried out, has been established. Healthcare professionals will be able to get vaccinated first while being an example and the main source of knowledge for patients. In this context, patient education is essential – making them aware of the importance of immunization, their role in preventing COVID-19, and thus in restoring the quality of family, social, and economic life.



Medical rationales for vaccinations

Examples of viral pandemics in history and the use of vaccines with success

Vaccinations changed the history of the world. One of the diseases eliminated thanks to vaccination is smallpox, which was one of the greatest threats to human health and accompanied people for nearly 3,000 years. The disease was very severe – the average mortality rate was 30%, and of those who survived, many had visual defects and unsightly scars. In the 20th century alone, smallpox killed about 300 million people worldwide. The first effective vaccine against this disease appeared in 1796 thanks to the English doctor Edward Jenner, but the lack of massive and universal vaccination in the world did not interrupt the virus's circulation. It was only thanks to the introduction of the universal vaccination program 'True Smallpox Eradication Program' in 1967 in every corner of the world that enabled the World Health Organization (WHO) to issue the long-awaited message on May 8, 1980 – the world was free from smallpox.

Poliomyelitis, or widespread childhood paralysis, was one of the greatest threats to children and young people worldwide in the 20th century. The disease was easily transmitted from person to person, and although only about 1% of those infected developed symptoms of paralysis of the limbs, and sometimes paralysis of the respiratory muscles leading to death, the mass incidence of the disease meant that in 1988 every day around the world 1,000 children underwent paresis and paralysis. The poor epidemic situation in the field of widespread childhood paralysis in the world was the reason for the launch of the World Initiative for the Eradication of Poliomyelitis in 1988. Since then, 2.5 billion children in over 200 countries were vaccinated worldwide with the help of 20 million volunteers. As a result, in 2020, only two countries still suffer from poliomyelitis. As of December 9, 2020, there were 56 cases in Afghanistan and 82 in Pakistan. In more than 30 years, the number of poliomyelitis cases worldwide has been reduced by 99%, but the ultimate goal of eradicating the disease has yet to be achieved.

What has the history of fighting smallpox and poliomyelitis taught us? Both examples show that the production of an effective vaccine is only the beginning of the path to increasing population immunity. Mass vaccination is the only way to stop the circulation of the virus and prevent further infection of hundreds of thousands of people.

In the modern world, thanks to modern communication and the ease of moving from one corner of the world to another, it is difficult to achieve the success of local programs. Therefore, only global action will allow the virus to be eradicated and the history of a given disease to be completed. The example of poliomyelitis shows that if contamination occurs in one region, even remote from us, it still poses a threat to the rest of the world, necessitating continued mass immunization.

Why is the vaccine the best support to fight viral diseases?

Viruses that can cause disease in humans are those that, by finding a way to enter the cell through the receptor, multiply inside the cell, using its resources. The viral replication cycle is closely related to the metabolism of the cells in the infected organism. So far, few drugs are effective against the viruses inside our cells. The available ones are directed against specific viruses (e.g., herpes, HCV, HIV) and act on specific enzymes. The drugs used so far to treat COVID-19 are effective only in the first phase of infection, inhibiting viral replication, which is most intense before symptoms appear. So far, however, there is no drug with very good efficacy that would show effect after the first week of the disease.

The immune system can effectively protect us against infection with pathogenic viruses, but only if it has acquired this property through prior contact with the virus or its fragment. Vaccinations are the safest way to acquire a controlled resistance to infection. A vaccine is a biological preparation that introduces antigens against which immunity is to be generated. It presents to the immune system the elements of the virus that it wants to recognize. Re-contact with the virus is no longer a surprise to the organism, and the antibodies and sensitized cytotoxic lymphocytes produced by vaccination protect the vaccinated person against infection.

Many viruses that cause human disease are transmitted by airborne droplets, airborne transmission, or direct contact between an infected person and a sensitive person. Outbreaks, epidemics, and even pandemics arise among vulnerable people. If an infected person appears among those who are immunized, she/he will not infect them. Mass immunization of the majority of society leads to the development of population immunity, also known as collective or herd immunity. In such a community, the infectious agent, unable to find sensitive organisms in which it could multiply, loses the possibility of transmission between persons. Therefore, population immunity offers protection to people who, for various reasons, cannot be vaccinated or for whom the vaccine is ineffective.

The course of the epidemic depends on the mutual proportions of infecting, susceptible, and convalescent people.



In the absence of immunization, a reduction in the number of cases occurs when the number of susceptible people decreases, and the number of convalescents who have acquired immunity in a natural way increases.

The use of vaccinations accelerates the increase in the number of resistant people (vaccinated people, like convalescents, acquire immunity) while reducing the number of susceptible people. As a result, the epidemic loses the conditions for further spread

The scale of the current pandemic, including the number of victims, attempts to fight it, and the lack of effective drugs

In December 2019, there were rapidly spreading outbreaks of unspecified severe viral pneumonia in Wuhan, China. The etiological factor of these diseases turned out to be a new coronavirus, the transmission of which has not been found in the human population so far. The World Health Organization named it SARS-CoV-2 (Severe Acute Respiratory Syndrome CoronaVirus-2) and COVID-19 (Corona Virus Disease-2019) – the disease it causes. On March 11, 2020, WHO announced the COVID-19 pandemic. Soon its epicenter moved from Asia to Europe and North America.

In the spring and summer of 2020, the greatest number of cases outside the USA was recorded in Italy, Spain, France, and the United Kingdom. At that time, Poland was one of the countries with one of the lowest daily numbers of positive results detected, which was tried to be explained with hypotheses about the influence of previous vaccination against tuberculosis or genetic factors. In retrospect, it is known that early restrictions were imposed, including primarily the closure of schools and other places, increasing the risk of transmission of infection. Until September, the daily number of identified infections did not exceed one thousand. However, at the beginning of the school year, there was a sharp increase in the number of infections, which on November 7 reached nearly 28,000 identified positive results for SARS-CoV-2. At the beginning of December, the total number of cases identified in Poland exceeded one million. However, it is estimated that the actual number of people who had contact with the coronavirus and acquired at least temporary immunity is 5-10 times higher. However, this is not enough to reach the threshold, ensuring population immunity in 2021. It must not be forgotten that the process of acquiring immunity through the further spread of SARS-CoV-2 in society will cost many people deaths. It is estimated that in November alone, about 20,000 people died due to COVID-19, and at least twice as much died due to the pandemic's disruptions in accessing healthcare facilities.

According to the analysis of hospitalized patients registered in the SARSTer database, the COVID-19-related mortality was 6.2% and 7.3% when considering only the adult population. However, mortality clearly increases after the age of 60. Every fifth person over 80 who requires hospital treatment dies, and among patients requiring mechanical ventilation (connection to ventilators), the mortality rate reaches 67%. Therefore, halting the spread of the pandemic and related deaths requires accelerating the development of population immunity through mass vaccination. During the pandemic, mainly based on clinical experience, the use of many drugs was proposed. No doubts as to the effectiveness and safety are raised only in case of the use of oxygen therapy and low molecular weight heparin in patients requiring hospitalization. However, it is supportive treatment.

The lack of optimal, causal COVID-19 therapy is an additional, powerful argument for intensifying preventive measures, emphasizing vaccinations.

How long are we likely to wait for the effect of vaccination on SARS-CoV-2? How long is the effect? And how does mass vaccination coverage (population vaccination coverage) contribute to these issues?

Pandemic and the unpredictable course of COVID-19, over 7% mortality in the age group 60–80 years and nearly 20% in the age group over 80 years, difficult to understand and complex pathogenesis of infection, lack of effective drugs and negation of the existence of the SARS-CoV-2 virus by specific environments is the basis and target for all activities necessary to inhibit the spread of infections. The primary goal is to achieve population immunity, which is guaranteed by patients who will never become infected for unknown, possibly genetically determined reasons, patients who have contracted COVID-19, and patients who have been vaccinated. As mentioned above, undoubtedly, the worst method of achieving population immunity is to allow the infection to spread freely in the population. This leads to large human losses and is a massive burden on a given country's health service and economy. There is also no guarantee that all those infected will develop immunity, nor there is certainty about how long it will last. The data on the nature, degree, and duration of humoral and cellular immunity and its dependence on the presence or co-existence of other diseases, other preventive vaccinations, age, race, sex, genetic characteristics, or even eating habits are still incomplete, and sometimes even contradictory. It was confirmed that the immune response to SARS-CoV-2 infection varied significantly in terms of time, quality, and quantity between individual patients. This heterogeneity



is a specific feature of infection with this virus. It is known that neutralizing antibodies to SARS-CoV-2 persist for at least six months. Historically, we know that in patients with SARS-CoV-1 infection, high titers of neutralizing IgG antibodies were maintained for five months and then decreased to undetectable values within 2–3 years. However, in patients infected with another coronavirus – MERS, the presence of neutralizing antibodies was observed 34 months after the disease. However, it should be remembered that the detection of neutralizing antibodies in the IgG class is not synonymous with the persistence of the immune response, just as the absence of these antibodies is not the same as the absence of a permanent immune response. This is due to the existence of, in addition to the humoral immunity conditioned by antibodies, the cellular immunity related to the activity of T lymphocytes.

Binding data on the persistence of the immune response after SARS-CoV-2 infection, and also after vaccination, will be obtained in 2–3 years. Regarding the time needed for immunity after vaccination, people vaccinated against SARS-CoV-2 with an mRNA-based vaccine did not achieve high levels of neutralizing antibodies until seven days after the second vaccination. However, it is important that it concerned over 90% of people.



mRNA technology and its application in vaccination

Principles of specific immunity – active and passive

The immune system uses a number of mechanisms to protect the body against microbes. These mechanisms are divided into non-specific (congenital) and specific (acquired). Non-specific mechanisms are fully developed and practically unchanged throughout a person's life (many of them are already active before birth), so they are fully operational before microbes enter the human body. Unfortunately, this type of immunity is sometimes insufficient to suppress microbes and does not retain permanent immune memory.

Specific immunity develops only 10–14 days after the penetration of microorganisms, but it is very effective and precise – unlike the non-specific response, the activation of which is associated with tissue damage. Specific immunity works with almost surgical precision, effectively eliminating only microorganisms and cells infected by them. Two types of lymphocytes participate in specific immunity – T and B lymphocytes. For simplicity, only the mechanisms by which B lymphocytes participate will be described. On the surface of these cells, there are receptors (called immunoglobulins or surface antibodies) that are able to recognize (bind) specific fragments of microorganisms (so-called antigens) in an amazingly specific way.

To put it simply, this means that a given B-cell receptor can bind strongly to only one antigen. Each B lymphocyte has tens of thousands of these receptors in its membrane, but they are all identical, that is, only capable of recognizing one antigen. Hundreds of millions of B lymphocytes are produced in the marrow every day, each of which may have completely different surface antibodies, so each of these cells can recognize different antigens.

At the time of the first contact with a microbe, only a handful of B lymphocytes in the human body could recognize the microbial antigens. Only during the infection, the few B lymphocytes are activated in the lymphatic organs, which starts the multistage process of transforming these cells into plasma cells, releasing soluble (secreted outside the cell) antibodies. The first step in this process is the intensive division of the lymphocytes, which recognizes the antigen with low affinity.

In the course of these divisions, changes in the structure of antibodies occur, which affect their specificity, i.e., the

ability to recognize an antigen specifically. These changes are random and lead to the generation of millions of diverse B lymphocytes capable of producing antibodies with different specificities. Only a few of these cells can produce such antibodies that will specifically recognize the antigen of the microorganism, and their multiplication and transformation into plasma cells occur as a result of further selection processes. The number of these cells increases to many millions, and the soluble antibodies produced by them bind to the surface of microorganisms and eliminate them from the body (most often not directly, but with the participation of non-specific mechanisms, e.g., in the process of phagocytosis, or as a result of activation of the complement system). Unlike B lymphocytes, which release antibodies, T lymphocytes are activated into cells that are able to kill cells infected by microbes directly. After eliminating the microorganism, most lymphocytes die, and only a few memory lymphocytes remain (which can survive in the body for several dozen years). These cells already have developed antibodies that recognize the antigens of the microorganism with high affinity and can rapidly become involved in the body's defense when repeatedly exposed to the same pathogen.

Exactly the same mechanisms as those needed to develop active immunity naturally occur in the body after administering the vaccine. The vaccine also activates B lymphocytes and leads to changes in 'refining' antibodies and plasma cells' formation.

The difference is that one does not have to be infected with the vaccine to acquire immunity (some severe infections may lead to permanent disability before immunity develops, or even death).

The immunity produced by vaccination is called active artificial immunity. There is another type of immunity – passive, based on administering antibodies isolated, for example, from a convalescent to a sick person or a person susceptible to infection. Unlike active immunity, passive immunity is short-lived and lasts up to several months.



Vaccine types

A vaccine is a biological preparation, the task of which is to imitate an infection with a microorganism and thus obtain immunity similar to the passing of a real disease, but in a much safer way. The vaccine may contain live, weakened or dead microorganisms or their fragments (e.g., mRNA vaccine). Vaccines containing virus fragments are considered very safe, and the technology of their production has been developed for about 20 years. In the case of the SARS-CoV-2 virus, which causes COVID-19, this type of vaccine is most intensively developed.

mRNA vaccines

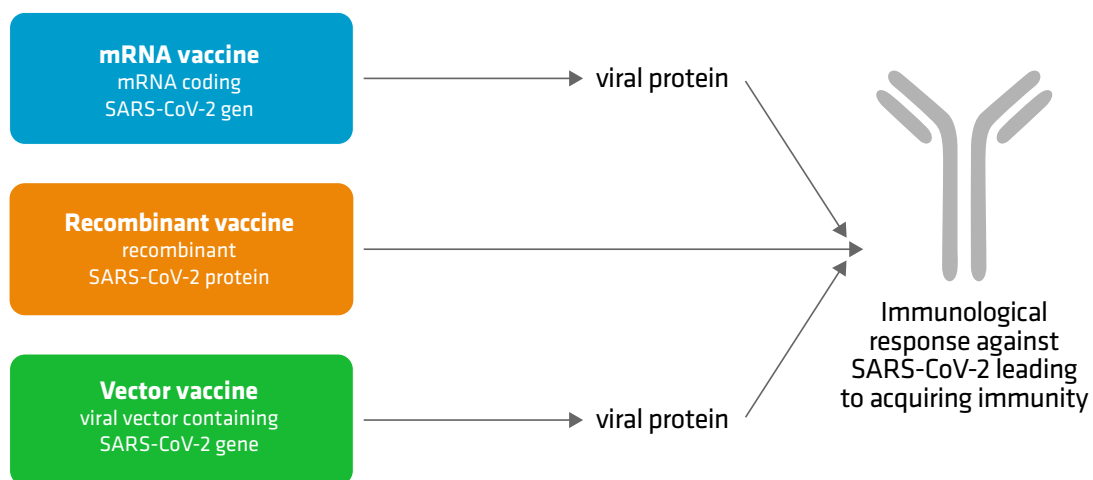
Such a vaccine uses ribonucleic acid (RNA) as a template for producing viral proteins intended to trigger antibodies' production. The RNA itself administered in the vaccine is not stable and degrades rapidly (therefore, low temperatures are required for its storage). In the case of an mRNA vaccine, the virus's genetic material never becomes integrated into the human genome. Examples of such vaccines are those obtained against SARS-CoV-2 by Pfizer/BioNTech and Moderna.

Recombinant vaccines

Recombinant vaccines are created by incorporating the genetic material of a microorganism into mammalian cells or yeast cells. The resulting recombinant proteins are isolated and purified and then administered to the patient to induce antibodies' production. These are classic vaccines developed by many companies against SARS-CoV-2, but none of them has yet been approved.

Vector vaccines

In the vector vaccines, the active viruses were modified to minimize the risk of infection. It is often a virus that safety and applicability in vaccines have been confirmed in the past or viruses not present in humans. These viruses are modified to trigger the production of a protein from the organism against which immunity is to be built when administered as a vaccine. Examples of such vaccines are those obtained against SARS-CoV-2 by AstraZeneca and Johnson & Johnson.



mRNA and vector vaccines contain genetic material of the SARS-CoV-2 virus, from which in the organism a viral protein is created and recognized as an antigen. This leads to acquiring immunity against the virus. A recombinant vaccine directly contains the viral protein. Therefore, there is no stage of its production by the human organism.

Figure 1. Vaccine types



What is mRNA technology (explaining mechanics in the context of genetics)?

Expression of genetic material.

mRNA – the biological role

In eukaryotic cells (including all humans, animals, and plants), the genetic information about proteins is encoded in enormous DNA molecules called chromosomes. For a given protein to be synthesized in a cell, the appropriate chromosome fragment called a gene must be transcribed into mRNA sequences, constituting a specific cellular 'protein recipe'. This 'recipe' is transported from the cell nucleus to the cytoplasm, where the process of translation takes place, i.e., the translation of the genetic code written

in the form of RNA sequences into the amino acid sequence of proteins. Based on one mRNA molecule, many molecules of a given protein can be created – just like in the kitchen, one recipe can prepare a given dish many times. Yes, to put it simply, with mRNA's help, proteins are created in our cells, which are involved in almost all processes taking place in our bodies.

RNA is unstable. When it does its job, and the protein is made, RNA is enzymatically degraded in cells by enzymes called ribonucleases, and the resulting nucleotides are used by the cell. So, it can be said that there is no trace left of the degraded mRNA, except for the protein it encoded.

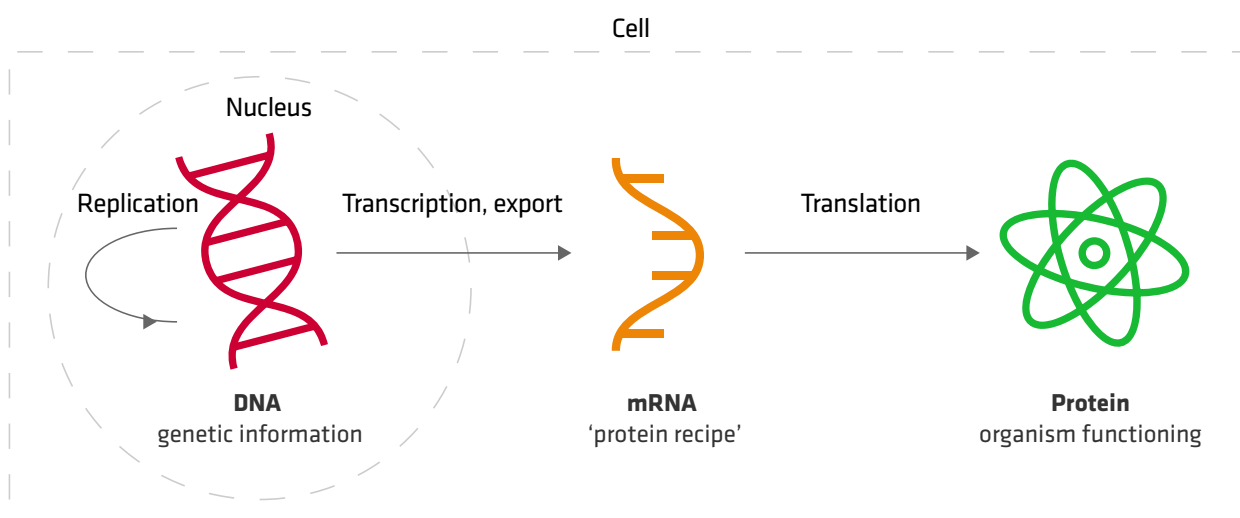


Figure 2. Expression of genetic information from DNA, by mRNA, to proteins

Development of gene therapy

Most traditional drugs are small-molecule chemicals that interact with various proteins to affect their activity. However, many diseases are challenging to treat with conventional drugs (e.g., cancer, genetic disorders, some viral diseases). Therefore, already in 1970s, the concept of gene therapy was created, in which information about a therapeutic protein is delivered to cells in the form of a genetic recipe.

Gene therapy can be performed in two ways: by providing DNA or mRNA encoding a given protein. Initially, scientists were inclined to use DNA. Still, for the genetic material to be expressed in the form of DNA (i.e., to produce mRNA and then proteins on its basis, see Fig. 2), it must be integrated with the patient's genetic material. Even nowadays, it is not effective enough and difficult to control. It is entirely different from mRNA expressed in the cytoplasm. mRNA never reaches the cell nucleus, the effect is transient, and the mRNA itself is a rapidly degrading molecule.

The most important thing, however, is that in human cells, there is no mechanism for transcribing sequences from mRNA to DNA and integrating such DNA into the genome. This means that incorporating the viral genetic material from the mRNA vaccine into the human genome and influencing it is absolutely impossible, making mRNA therapy completely safe in this respect.

The last 20 years have been marked by intensive work on the development of therapeutic mRNAs and several discoveries have enabled mRNA use in therapy. The main achievements in this field include increasing the stability of mRNAs, reducing their immunogenicity (i.e., the ability to induce a response from the immune system), or solving the problem of mRNA delivery inside cells. All this so that enough protein is produced from as little mRNA as possible to have a therapeutic effect.



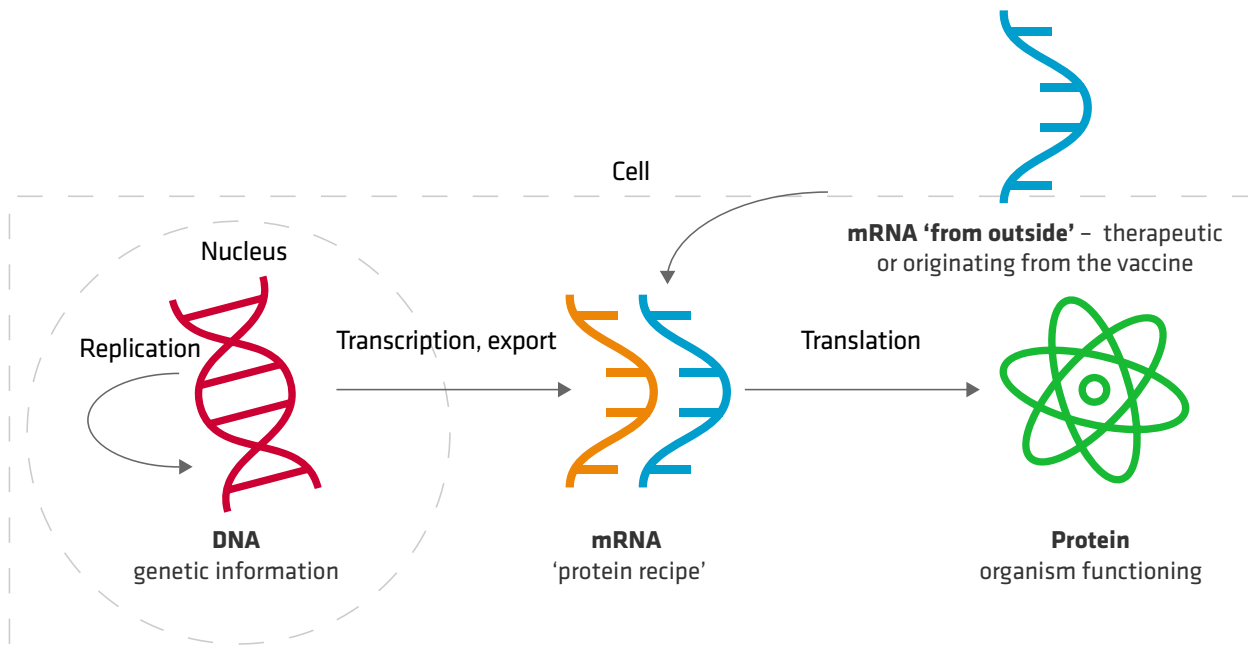


Figure 3. Therapeutic protein from mRNA supplied from the outside is produced by a natural translation process occurring in the cell.

Therapeutic mRNA

mRNA therapy consists of delivering mRNA encoding a therapeutic protein to the patient's cells. It could be a protein that is not working correctly in the given patient or is being made too little because of the disease. It can also be a protein characteristic of some pathogen which task is to activate the immune system against that pathogen. The latter case is used in the development of an mRNA vaccine.

One of the great advantages of this technology is that by changing only the nucleotide sequence in a therapeutic mRNA once developed, we can obtain almost any protein because the method of obtaining and purifying mRNA of any sequence is the same. mRNA is received in a test tube by a biochemical reaction, and its production can be easily scaled up. The development of a therapeutic against one disease makes developing another one against other diseases much more straightforward, cheaper, and quicker. This is especially important in a pandemic situation. Clinical trials for mRNA vaccines against cancer and non-SARS-CoV-2 viruses, as well as mRNAs that treat rare genetic diseases, have been underway in many companies for over ten years. This explains why we have got the first SARS-CoV-2 vaccines so quickly and why mRNA vaccines are winning this race. It also gives hope that the acceleration of work on this technology caused by the pandemic will translate into progress in treating other diseases in the near future.

Why is the mRNA vaccine safe?

- The genetic material of the virus contained in the vaccine cannot modify a patient's DNA
- a recipe is provided for only one virus protein (out of several dozen viral proteins and the genetic material of the virus necessary for its existence), thanks to which there is absolutely no possibility of infection
- mRNA is a natural component of our cells
- mRNA lasts a short time (hours) in cells, then it degrades into harmless, natural components
- a very small dose of the vaccine is enough to produce a therapeutic effect. E.g., in the Pfizer / BioNTech vaccine, it is 30 micrograms, which is over 100,000 times less than the sugar in a teaspoon
- therapeutic mRNA, its effectiveness and safety have been studied in patients in the context of various diseases for many years (first clinical trials using mRNA¹: 2001; direct administration of mRNA to a patient²: 2009)

1) Clinical trials started in 2001 – the first delivery of mRNA to dendritic cells and introduction of these cells into the patient's body described by Heiser, A. et al. Autologous dendritic cells transfected with prostate-specific antigen RNA stimulate CTL responses against metastatic prostate tumors. *J. Clin. Invest.* 109, 409-417 (2002).

2) Clinical trials started in 2009 – first direct injection of mRNA into the patient's body described by Weide, B. et al. Direct injection of protamine protected mRNA: results of a phase 1/2 vaccination trial in metastatic melanoma patients. *J. Immunother.* 32, 498-507.



SARS-CoV-2 as the cause of a global pandemic

What are coronaviruses?

Coronaviruses are a large family of RNA viruses that include many species that infect humans and animals. Coronaviruses consist of a large (approx. 30,000 nucleotides) molecule of single-stranded RNA closely bound to the N protein, which forms the core that protects and stabilizes this sensitive molecule. This core is surrounded by a membrane in which the virus's structural proteins are embedded – envelope protein E, membrane protein M, and the most important – the protein S (spike), responsible for recognizing the host cell and initiating the infection process (Fig. 4). While coronaviruses exhibit greater variability than DNA viruses, or even more so with higher organisms, they are far from other RNA viruses, such as the influenza virus, in this respect. Contrary to them, they have a system for correcting errors arising in replicating the genetic material. As a result, they change significantly more slowly.

The first species of coronaviruses were discovered in the 1940s in samples taken from sick animals. Further research showed that these viruses can be pathogenic, causing diseases of the respiratory and digestive systems, viral hepatitis, or infectious peritonitis. However, different species of these viruses vary in virulence – while infection with some does not lead to serious clinical conditions, infection with others invariably leads to death. In the 1960s, it was

discovered that some members of the coronavirus family could also infect humans. Two species – HCoV-229E and HCoV-OC43 – were associated with the common cold and diseases of the upper and, less frequently, lower respiratory tract. For many years, the coronaviruses were not the subject of detailed studies because their clinical significance was low. However, at the end of 2002, one of the animal viruses, SARS-CoV beta-coronavirus, became capable of infecting humans. In the 2002-2003 season, the virus infected about 8,000 people, causing severe acute respiratory syndrome (SARS), with a high mortality rate of approximately 10%. Fortunately, the virus's ability to travel between humans and humans decreased drastically with the advent of higher temperatures, and structured countermeasures such as contact tracing and isolation effectively cut infection pathways. As a result, the SARS epidemic was extinguished entirely. The advent of SARS-CoV electrified the world of science and medicine. It was proven that some coronaviruses have a high ability to spread from animals to humans and can pose a real epidemic and medical threat. Extended research resulted in the identification of two more 'human' coronaviruses – HCoV-NL63 and HCoV-HKU1 – which in the vast majority of cases cause relatively mild respiratory disease. Also, at that time, the first research was initiated to develop effective methods of preventing coronavirus infections and their therapy – vaccines and active substances. However, they were largely dropped in the preclinical stage as the SARS-CoV virus disappeared.

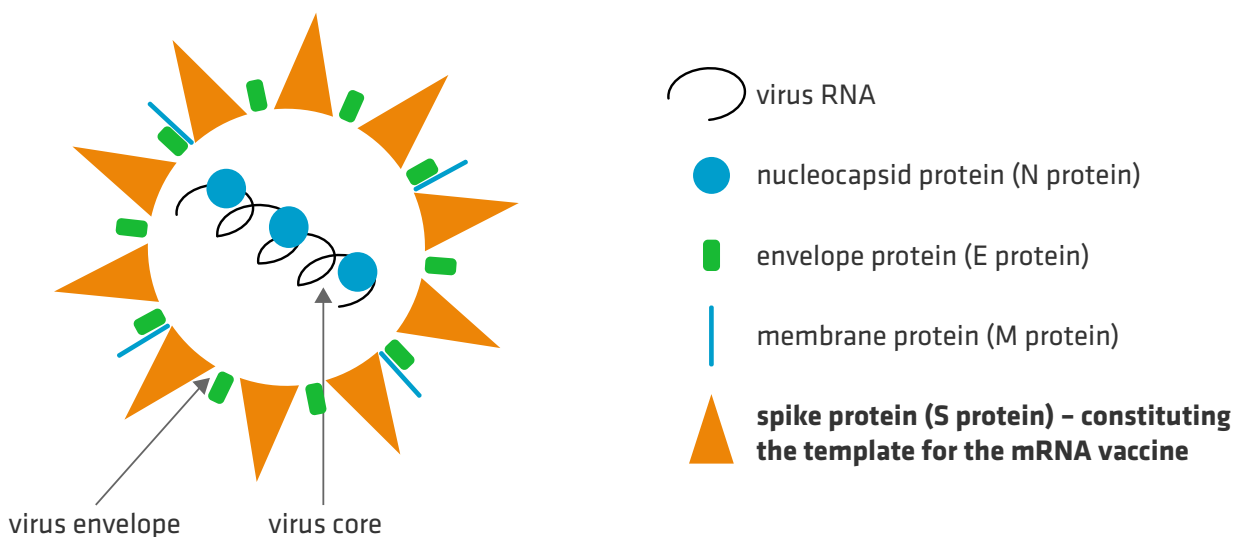


Figure 4. A simplified SARS-CoV-2 structure



Another major coronavirus-related epidemic occurred in 2012 when human infections with the highly pathogenic MERS-CoV species were detected in the Arabian Peninsula. This virus's infection leads to the so-called Middle-East respiratory syndrome (MERS), characterized by a high mortality rate of 35%. Due to frequent travels MERS-CoV infections were identified in various Asian countries, as well as in Europe and Africa; however, the virus is relatively difficult to transmit from person to person. Most infections occur due to human contact with camels, which are the main reservoir of MERS-CoV. Consequently, while MERS-CoV is with us today, its occurrence is primarily restricted to the Arabian Peninsula. As in the case of SARS-CoV, after the appearance of the MERS virus, work began on effective methods of preventing and treating its disease. Simultaneously, voices began to appear more and more often, suggesting that zoonotic coronaviruses could pose a significant threat in the coming years. Analyses of samples from wild animals showed that bats were the true reservoir of coronaviruses. Their organisms contain thousands of varieties belonging to this family of viruses, which continuously adapt to the effective immune system of animals and are continually evolving. Considering the high risk of transmitting these viruses to humans and increasing human interference in the natural environment, this threat has become very real.

SARS-CoV-2

In 2019, another animal coronavirus gained the ability to spread to humans, as well as further spread human-to-human. On December 31, 2019, the first report of pneumonia cases of unknown etiology in the Hubei province was released. Ten days later, Chinese scientists published the entire genome sequence of the causative agent – beta-coronavirus. The International Committee on Taxonomy of Viruses named it SARS-CoV-2 and classified it under the Sarbecovirus subgenus, the same to which the previously discussed SARS-CoV belongs. The genetic relationship between these viruses indicates that while both viruses are derived from the same evolutionary lineage, SARS-CoV is not a direct ancestor of SARS-CoV-2. However, it should be remembered that the relationship among viruses is much more distant than that of other living organisms. At the genetic level, they are less similar to each other than humans are to mice.

The appearance of the SARS-CoV-2 virus in China initially aroused limited emotions in Poland. It was not assumed that it could reach our country or affect our lives to such an extent. However, it happened otherwise. After the initial wave of infections in Southeast Asia, a storm hit Europe that wreaked terrible havoc in some countries. The rapid spread of SARS-CoV-2 was driven not only by globalization and associated international transport but also by the virus's characteristics. It is worth mentioning the most important ones here: the virus is transmitted by droplets

without the need for close contact, the long period of incubation of the disease allows transmission over long distances, an infected person becomes contagious before the appearance of symptoms and a relatively high percentage of people pass the infection with mild symptoms or almost asymptomatic, which facilitates the spread of the virus.

But why has the SARS-CoV-2 virus stopped the world? Of course, it is a serious threat to life, especially among people at high risk. These include the elderly, people with cardiovascular diseases, people with obesity, cancer patients, people with type 2 diabetes, chronic kidney disease, and chronic respiratory diseases. The second problem is the epidemic spread of the disease. With such a high percentage of patients requiring hospitalization, the healthcare system is overloaded very quickly. Patients, who do not receive help, die both due to COVID-19 as well as for other medical conditions. The complicated clinical picture of COVID-19 aggravates the situation. Although the virus travels through the respiratory system, SARS-CoV-2 can infect many other organs. It can be found in the nervous system, heart muscle, vessels, pancreas, intestines, and many other parts of our body. In addition, in many cases, the virus modulates the immune system tragically, and our own immune system becomes a lethal threat to us. It should also be noted that the convalescence after SARS-CoV-2 infection is in some cases long-lasting, and in some people, the disturbing changes remain even after a mild disease. We still do not know if the traces of infection in some of the convalescents will be permanent. In Poland, an early and decisive reaction at the beginning of a pandemic, consisting in the introduction of the so-called lockdown, allowed for a significant reduction in the number of COVID-19 cases in the spring. The lack of rapid increases in the number of cases and victims of the disease, also observed in the summer, while returning to normalcy, gave the impression that the threat passed. On the other hand, the arrival of the autumn period began to favor the transmission of the virus due to frequent stay in confined spaces and the characteristics of the pathogen itself, as well as confusing COVID-19 symptoms with seasonal respiratory infections. As a result, a very dynamic increase in the number of cases was recorded, leading to a crisis in the health service and forcing the return of restrictions. While the number of cases is now lower than in mid-fall, it remains high, and the death toll remains shocking.



The complex nature of COVID-19 causes the conscious pursuit of the so-called population resilience can be considered a dangerous fallacy that leads to high deaths, healthcare system failure, and catastrophic economic consequences. It should be noted that the available data suggest that COVID-19 disease is not associated with the generation of a sustained immune system response to SARS-CoV-2, and the reports of reinfection are not optimistic in this regard.

Today, we are faced with the simple choice of getting vaccinated against COVID-19 or taking part in a difficult to predict lottery related to the disease and the further deepening of the economic and health crisis.

This choice is only possible thanks to international efforts, which have allowed vaccine research to be conducted at an unprecedented pace, but with an assessment based on the three most essential pillars: safety, immunogenicity, and efficacy. If we compare the multifaceted consequences of the disease and the potential side effects of vaccination, which do not differ from those seen with other vaccinations against viral diseases, the choice should seem simple.



Registration and marketing authorization of medicinal products in relation to SARS-CoV-2 vaccines

According to the current nomenclature, vaccines are a group of medicinal products (as opposed to medical devices and biocidal products). Although they do not treat, they meet the legal definition of a medicinal product because they protect vaccinated people against viral and bacterial infections. Even in situations where the vaccinated person becomes ill because of a weaker response from their own immune system, the disease's course will be much lenient.

Registration of a medicinal product (marketing authorization of a medicinal product)

Pursuant to the requirements of the pharmaceutical law, registration of a medicinal product is called marketing authorization. Admission to the market of a medicinal product is based on the declaration by a competent authority, based on the documentation submitted by the applicant, that the product is safe, effective, and of good quality. Positive evaluation of a medicinal product concerns the knowledge available at the time of issuing the

decision. The Marketing Authorization Holder (MAH, i.e., the company that applied for the marketing authorization of the medicinal product, usually its manufacturer) has a legal obligation to observe the medicinal product already on the market and respond to all new, relevant from the therapeutic point of view, information. As a result of the data collected this way, the medicinal product remains on the market or is withdrawn from it.

In the European Union, there are three routes for obtaining Marketing Authorization in several EU countries at once, which differ in the process, but the required documentation remains the same. It is also possible to obtain a marketing authorization at the national level (then it only applies to the country in which it was issued). In Poland, the decision-making body in this matter is the Office for Registration of Medicinal Products, Medical Devices, and Biocidal Products (URPL). Most of the SARS-CoV-2 vaccines will be assessed by the European Medicines Agency as part of the central procedure. If it is positively recommended, the vaccine will obtain marketing authorization from the European Commission (Fig. 5). This means that these vaccines will be authorized simultaneously in all European Union countries. More information on this procedure can be found on the European Medicines Agency website linked in the 'Verified Resources of Knowledge' appendix. In the event of free access to a medicinal product (e.g., to a vaccine against SARS-CoV-2), the Agency for Health Technology Assessment and Tariffication must give an opinion, which will reassess the effectiveness and safety in the defined indication for reimbursement, i.e., it will answer the question whether it is worth spending budget money for free vaccination of Polish citizens against SARS-CoV-2.

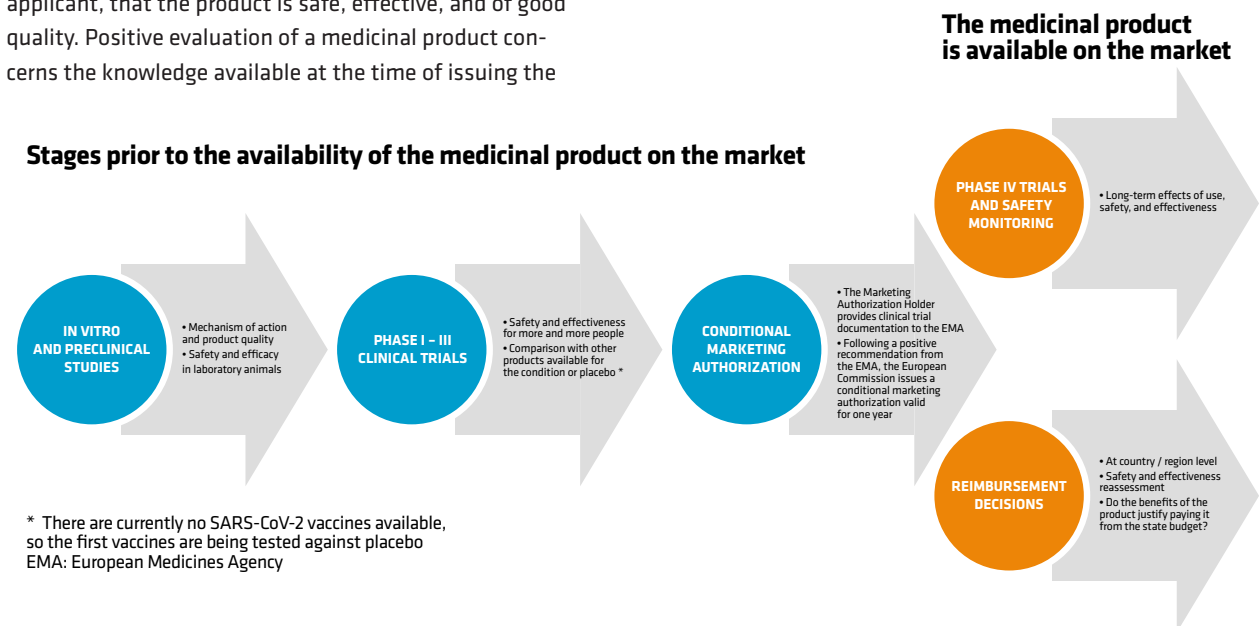


Figure 5. The process of evaluating a medicinal product before and after marketing authorization.



Competent bodies

Medicines licensing authorities are called competent authorities. Each country has a Registration Agency or Department within the Ministry of Health. In Poland, it is the URPL mentioned above. In addition, the European Union also has the aforementioned European Medicines Agency (EMA), which associates the competent authorities of 27 member states. Otherworld agencies that influence drug registration include the Food and Drug Administration (FDA) in the USA, Canadian Agency, Australian Agency or Japanese Agency. Of these, the FDA has the greatest reach and is the benchmark and legislative model for the registration proceedings conducted in the countries of the Americas, Asia, and Africa.

Conditional registration

Conditional registration is an important concept for SARS-CoV-2 vaccination. It allows the use of a medicinal product in everyday clinical practice based on less comprehensive studies than those necessary to obtain a standard marketing authorization. The conditional procedure is used in relation to medicinal products that, at the stage of phase I or phase II studies, have shown efficacy in the treatment or prevention of clinical situations in which there has been no proven effective treatment method so far, and the patients are in a state of the immediate threat to their life or health. To sum up, this method of registering a medicinal product applies to situations where it is not possible to compare a medicinal product with others because such products do not exist in a given indication. In the literature, such a situation is referred to as an unmet medical need. The reason for this decision is the ethical aspect. It is also worth noting that the conditional registration procedure is not new and was not created to fight the SARS-CoV-2 pandemic. This procedure has been in place since 2006, and in the first ten years of its application, none of the 30 conditional marketing authorizations issued had to be revoked or suspended.

Indications for the use of the medicinal product

The medicinal product can be used in clinical practice in accordance with the indications for use described in the summary of product characteristics. These indications are based on clinical trials conducted with the product. Sometimes the treating physician decides, at his own risk, to use a given product outside the indications for use included in the summary of product characteristics. This is an off-label use that carries a potential additional risk of use due to the lack of previous comprehensive clinical trials. However, it is unlikely that off-label use issues will apply to SARS-CoV-2 vaccination.

New medicinal product

A medicinal product that has just been authorized is admittedly a new product on the market, but it has undergone long tests in clinical trials. Positive results from large phase III trials with an appropriately selected control group are sufficient to apply for marketing authorization. Still, they are not the end of the road for a medicinal product. On the contrary, a product already admitted to trading is observed in everyday use (the so-called real-world experience). Its safety is closely monitored according to the applicable Polish and European legal standards. Often, products already authorized on the market are subject to phase IV clinical trials to gather additional information on the long-term safety and efficacy of the product. Such a study may be imposed by the competent authority that granted the marketing authorization or taken on the MAH initiative.

Clinical trials

Phase I – the medicinal product's safety is determined, and the optimal dosing regimens are established.

Phase II – the therapeutic efficacy and safety of the medicinal product are determined.

Phase III – confirms the effectiveness, safety, and dosing schedules.

Phase IV – these are the aforementioned post-registration clinical trials. They are therapeutic trials in medical practice, needed when changes are made in terms of indications, dosage, type of packaging, and changes in pharmaceutical form. Clinical trials in pregnant women are not carried out, but the safety of already authorized products in pregnant women is monitored.

Clinical trials conducted on children, the so-called pediatric clinical trial, rely on separate regulations.

Suspension and recall of a medicinal product

A medicinal product may be suspended or withdrawn from the pharmaceutical market by:

- Main Pharmaceutical Inspector – due to quality defects.
- President of URPL – if there are data about insufficient safety of use or therapeutic effectiveness. The Minister of Health substantively supervises both institutions, and the President of URPL is formally subordinate to the Prime Minister of the Polish government.



Collecting information about side effects, including vaccine side effects

In the event of adverse drug reactions to medicinal products, including post-vaccination reactions, the frequency and severity of adverse events are essential. Information on side effects and post-vaccination reactions is collected in Poland by:

- Office for Registration of Medicinal Products, Medical Devices, and Biocidal Products. Contact details of the Registration Office: fax 22-49-21-309 or e-mail: ndl@urpl.gov.pl. You can also contact the office using the Mobit Skaner mobile application or by traditional mail.
- Marketing Authorization Holders (as defined above; the Marketing Authorization Holder's name for a given product can be found in the Summary of Product Characteristics).
- PNational Institute of Hygiene – National Institute of Public Health – only post-vaccination reactions.
- Bodies:
 - State Sanitary Inspection – only post-vaccination reactions.
 - State Sanitary Inspection of the Ministry of the Interior – only vaccine reactions.
 - Military Sanitary Inspection – only post-vaccination reactions.

Side effects of medicinal products, including vaccines, are obligatorily reported by doctors, pharmacists, nurses, midwives, and paramedics. However, patients and their statutory representatives or actual guardians also have the option to report side effects to the above-mentioned authorities. Medical professionals should report severe side effects of medicinal products within 15 days from the date of receiving information about their occurrence.

However, the Act on infectious diseases requires to notify about vaccine adverse events (VAE) within 24 hours.

The Act of December 5, 2008, on the prevention and combating of infections and infectious diseases in humans, Journal of Laws 2008, No. 234, item 1570 provides as follows: Art. 21.1. A doctor or a feldsher, who suspects or recognizes the occurrence of an undesirable post-vaccination reaction, is obliged within 24 hours from suspecting its occurrence to report such a case to the state district sanitary inspector competent for the place of suspicion.

From a legal point of view, the notification must include:

- name of the medicinal product,
- description of the adverse reaction (at least one of the symptoms),
- patient data (initials, gender, or other identifying data of the patient),
- data of the reporting person (name, surname, address, telephone number, e-mail address).

However, the above requirements are too scarce to take optimal action and therefore, the addition of:

- the reason for administering the medicinal product,
- series,
- expiry date,
- pharmaceutical form,
- application routes,
- the type of dosage,
- other medicines used in this disease or coexisting diseases,
- the age, weight, height, and race of the patient.

References

- Pharmaceutical Law Journal of Laws No. 2001 No. 126 item 1381 with changes until 2020
- Regulation of the Minister of Health of October 2, 2018, Journal of Laws of the Republic of Poland, item 1994
- Act of November 6, 2008, on patient rights and the Patient's Rights Ombudsman /Journal of Laws of 2008, no. of 2012, item 159 and 742/
- Directive of the European Parliament and the Council 2005/28/EC – from January 29, 2006
- Regulation of the European Parliament and the Council / EU/No. 536/2014 of April 16, 2014.
- Directive of the European Parliament and the Council 2010/84/EU of December 15 2010, Regulation 1235/2010, Regulation 530/2012.
- Report of the European Medicines Agency on conditional marketing authorization 'Conditional marketing authorization. Report on ten years of experience at the European Medicines Agency' 2017.



Vaccination plan and importance of primary care physicians and nurses

How should I prepare to implement a vaccination plan?

The logistics and distribution of vaccinations against COVID-19 is a large-scale undertaking not yet noted in Poland's post-war history. Such a scope of activities has not been undertaken so far, not only in our country but also in the world. Issues related to the organization of vaccination campaigns are raised in various forums, including the European Commission forum. They include problems:

1. to ensure easy access to vaccines;
2. introduction of vaccines with different properties;
3. identifying the groups and people most susceptible to infection and the rates of disease severity and mortality in these groups;
4. ensure adequate storage and transport, particularly the cold chain, refrigerated transport, and storage options.

Planning is urgently needed. In the US, work began with a review of lessons learned from previous mass vaccination campaigns in the US and worldwide, including the 2009 H1N1 flu vaccination campaign and the 2013–2016 vaccination campaign during the Ebola outbreak in West Africa. Ethical principles and prioritization strategies have also been established as part of the allocation of other medical resources – including some recently developed to distribute rare hospital drugs for COVID-19.

The following conclusions were drawn from previous mass vaccination campaigns:

- the need to develop effective systems for tracing distribution, to ensure its timeliness and the appropriate quantity of vaccines supplied;
- the risk of 'unfulfilled promises' in relation to overstated plans and communication activities;
- ensuring up-to-date information on vaccine production, stocks, and forecasts through stronger and more formal cooperation between central actors and vaccine manufacturers;
- planning a number of vaccine delivery scenarios;
- consider using the infrastructure of a childhood immunization program as the basis of adult emergency immunization distribution programs;

- implementing limited vaccine supplies in a fair and transparent manner;
- using consistent, respectful, and accurate communication to earn, secure, and maintain trust.

On October 15, 2020, the European Commission presented the Communication from the Commission to the European Parliament and the Council on preparedness for the COVID-19 vaccination strategy and vaccine implementation. The Communication provides recommendations for member states that should start developing a common vaccination strategy to distribute vaccines. The member states should ensure, among other things:

- the capacity of the vaccination service to deliver the COVID-19 vaccine, including qualified personnel and medical and protective equipment;
- easy and inexpensive access to vaccines for target groups;
- distribution of vaccines, taking into account the different storage and transport needs, in particular the cold chain, low-temperature transport of products and storage capacity;
- clear information on the benefits, risks, and importance of the COVID-19 vaccine to gain public confidence.

National Immunization Program

On December 8, 2020, the National Immunization Program prepared by the Ministry of Health was published, taking into account the above recommendations for vaccine distribution.

Poland decided to enter into five vaccine purchase agreements: AstraZeneca (16 million), Janssen Pharmaceutica NV / Johnson&Johnson (16.98 million), CureVac (5.72 million), Moderna (6.69 million), Pfizer / BioNTech (16.74 million).

The Material Reserves Agency will be responsible for the correctness and efficiency of distribution. Storage capacity has been secured, enabling the expected supply of vaccines to be stored in the cold chain (2–8°C) and low temperatures (-75°C) conditions. Logistics centers have been selected, which will provide storage and distribution facilities. Transport will be carried out using a specialized fleet of vehicles with a refrigeration system or special transport devices that maintain a specific low temperature.

The entire process is based on well-functioning distribution networks of pharmaceutical wholesalers. Vaccination points will place orders in a dedicated IT system, enabling the monitoring of orders and the status of deliveries. Additional equipment required by vaccine manufacturers will be secured in the form of syringes, needles, gloves, surgical masks, swabs, and saline solution. Their distribution will



be correlated with the supply of vaccines. Vaccine tranches from individual manufacturers will be divided to secure both doses required for vaccination from one shipment. This will ensure that the patient can be revaccinated after 3 or 4 weeks, in accordance with the manufacturers' guidelines.

Poland focused mainly on the existing network of vaccination points operating primarily within primary health care. It employs medical personnel with many years of experience in the field of vaccinations, meeting all legal requirements in terms of competencies and conditions necessary for the operation of such facilities. The outpatient specialist care centers and other medical facilities supplement the primary health care. Additionally, mobile vaccination teams will be created to perform vaccinations at the patient's place of residence or stay, as well as vaccination centers in reserve hospitals. The vaccination procedure will be carried out in two groups: individually and in groups. Individual procedures will be performed at the vaccination points, while group vaccinations are designed, among others, for health care workers, uniformed services, residents of nursing homes, care and treatment facilities, and nursing and care facilities. Depending on the logistic possibilities and the manufacturer's recommendations, group vaccinations can also be performed in hospitals divided into three groups:

- 1) Node Hospitals vaccinating the staff of medical entities and pharmacies
- 2) Pediatric and oncological hospitals vaccinating only their staff
- 3) Care and Treatment Institutions vaccinating charges and their own staff

Due to its mass, scale, vaccine production, and distribution procedures, the vaccination campaign will be phased. Based on four criteria, the order of the priority groups that will be vaccinated at each stage was established. The risk of exposure to infection, serious illness, death, socioeconomic status, and transmission was taken into account.

- Stage 0: employees of the health sector (medical personnel, employees of social welfare homes and municipal social welfare centers, as well as auxiliary and administrative personnel in medical facilities, including sanitary and epidemiological stations).
- Stage 1: residents and employees of the nursing home, care and treatment facilities, nursing and care facilities, and other places of stationary stay; the elderly over 60 years of age (starting with the oldest); uniformed services, including territorial defense forces.
- Stage 2: key professional groups: employees of the education sector, employees of the critical infrastructure sectors, public transport, officials directly involved in combating the epidemic (e.g., employees of epidemiological and sanitary stations); people under 60 years of age with chronic diseases that increase the risk of severe COVID-19.
- Stage 3: entrepreneurs and employees of sectors closed under regulations on establishing certain restrictions, orders, and bans in connection with the epidemic's occurrence; widespread vaccination of the rest of the adult population. At this last stage, vaccination will be for those over 18 years of age who do not have any underlying medical conditions and do not belong to any of the groups above.

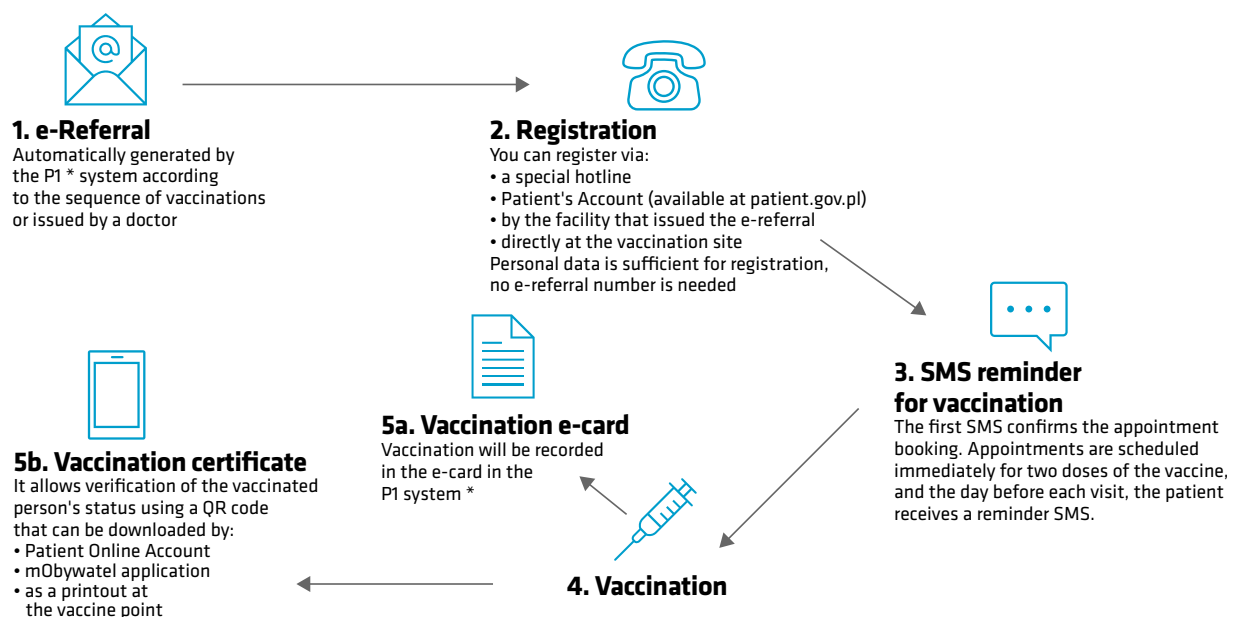


Figure 6. Vaccination course from the patient's point of view.



The role of primary care physicians and nurses in patient education and activities for high vaccination coverage

In the health policy of European societies, immunization is the most effective intervention in preventing infectious diseases. Immunization coverage depends largely on the education of people subject to vaccination, which should be attended by medical professionals of various specialties, including nurses performing vaccinations. The education of medical staff is also extremely important, which translates into patient education. The continuous development of the COVID-19 vaccination program requires the medical staff - the doctor and the nurse - to keep their knowledge of vaccination up-to-date. Communication skills and building an atmosphere of trust are essential to convey this knowledge to the patient. Educational tools worth using in promoting SARS-CoV-2 vaccination in society include:

- Communications for patients - preventive vaccinations bring many individual and social benefits, primarily preventing COVID-19 and often fatal complications. They influence the evolution of population resistance. They generate savings on social and health benefits and for the health care system thanks to the reduction of the number of medical visits and the decrease in expenses incurred on hospitalization. Thus, they improve family and social life quality, preventing exclusion due to illness and its consequences.
- Messages and materials for doctors and nurses:
 - Information for healthcare professionals on COVID-19 vaccines, based on current clinical trial results and reports
 - Educational materials on how to deal with vaccine-negative patients
 - Patient materials, e.g., vaccine videos, a COVID-19 immunization guide (electronic and printed) describing each vaccine and answering frequently asked questions from patients about immunization
- The use of new technologies - chatbots for medical staff and patients, creating an application for patients informing them about the latest news on vaccinations, which will also have a motivational function, e.g., showing the vaccination rate in the area where the logged-in person is (application similar to ProteGO safe).
- Social media - the use of tools such as Facebook (dedicated profile), Twitter, Instagram, YouTube, TikTok.

The model for promoting vaccination against COVID-19 should be based on effective and long-term activities carried out by government institutions with the support of non-governmental organizations and scientific societies, as well as on cooperation with patients who can inform the local community about vaccination and encourage its implementation.

Recommendations for the education of medical personnel and patients

Education of medical personnel

One of the groups most important to the success of educational campaigns to promote vaccination against COVID-19 is healthcare professionals:

- on the one hand, doctors and nurses are the main source of information for patients on vaccination, and most patients decide to vaccinate after obtaining a medical or nursing recommendation;
- on the other hand - coronavirus, as an infectious disease transmitted mainly by airborne droplets, may be a serious epidemiological and organizational problem in health care facilities.

Strategies for promoting vaccination among healthcare workers against COVID-19 should include, in particular:

- Educational campaigns on vaccination against COVID-19 (lectures, brochures, newsletters distributed by e-mail and in a traditional way, posters) describing:
 - The risk of disease and complications among staff and patients
 - Consequences of an outbreak in health care institutions: financial (the cost of controlling an epidemic among patients, including temporary suspension of service activities, absenteeism, staff shortages, the need to organize replacements), image (loss of patient trust), and legal (claims for damages)
 - COVID-19 vaccines: efficacy, safety, differences between the available preparations
- Facilitating access to vaccinations in the workplace:
 - Free vaccines for staff
 - Vaccination against COVID-19 should be recommended to all people working in medical care facilities, both having direct contact with the patient and technical and administrative staff
 - Vaccinations at a place and time convenient for employees
 - Easily accessible information on vaccination
- Motivating oneself to vaccinate:
 - Examples of vaccination of chief physicians and/or other local opinion leaders
 - Administrative requirement to undergo vaccination when employed in a specific position
 - Financial incentives



Patient education

The National Immunization Program envisages a number of educational initiatives for patients:

1. **Creation of a knowledge base for patients** – in order to implement a responsible information policy, it is necessary to create a credible and widely available knowledge platform where citizens will find all the necessary information on vaccination against COVID-19, both theoretical and practical.

2. **Creation of FAQ section** – section of frequently asked questions. The formula of questions and answers will allow one to provide information as closely as possible to people's experience and translate procedures and instructions into everyday situations.

3. **Automation of the information process for patients** – in urgent situations requiring an individual approach, citizens will be able to contact the hotline run by specialists from the National Health Fund.

4. **Experts** – an important role in shaping the information policy will be played by experts – scientists, medics, and epidemiologists. They are not only a valuable source of knowledge and analyzes that allows the rulers to make responsible decisions but also play an extremely important role in the field of social education.

5. **Information:** information campaign in the media and on the Internet.

6. Additionally, **the use of new technologies** (mobile applications, robots collecting up-to-date information and transmitting it to citizens) should be considered.

7. **Motivational incentives**, e.g.:

- The vaccinated person will be able to count on faster service in health care facilities; should be treated as if they tested negative for coronavirus.
- Release the vaccinated person from the sanitary regime.
- Partial release from quarantine. If the person we live with, a parent, spouse, or child, becomes infected with coronavirus, the vaccinated people living with them will not have to undergo quarantine.
- When there are restrictions on quarantine after returning from abroad, vaccinated persons will be released from this obligation.



Glossary

Amantadine: an antiviral drug that stops the multiplication of the virus (mainly influenza)

Etiological factor: causes the formation of the disease

DNA: deoxyribonucleic acid in which human genetic information such as eye or hair color is stored. It is stored in the nucleus of each cell

Microbes: Collective name for organisms that can be observed under a microscope

Epidemic: Increased incidence of an infectious disease in an area

Genome: the entire genetic material of an organism

Low molecular weight heparin: a substance that inhibits blood clotting, used in medicine for anticoagulant purposes

Heterogeneity: non-homogeneity, diversity

Immunogenicity: a property of a substance that allows it to trigger an immune response against itself

Isolation: isolating a person or group of people who are sick or suspected of having an infectious disease. Used to prevent the transmission of diseases from one patient to another

Casuistic: based on cases or examples

Drug: a substance that inhibits the symptoms and development of the disease by modifying physiological processes

Lymphocytes: cells of the immune system that provide a precise response to infections

mRNA: messenger RNA: ribonucleic acid (RNA) serving as a template for the formation of proteins by cells

Nucleotides: organic chemical compounds that are the basic building blocks of nucleic acids (DNA and RNA)

Plasma: the basic fluid component of blood that forms the environment for blood cells and other blood components

Pandemic: A larger-scale infectious disease epidemic that has spread to many continents and even the world.

Pathogenicity: ability to initiate disease

Medicinal product: A substance or mixture of substances with properties to prevent or treat disease in humans or animals

Antibodies (immunoglobulins): proteins that recognize and bind to things that are foreign to the body (e.g., bacteria) and allow them to be eliminated by the immune system. The most common type of antibody is IgG

Remdesivir: an antiviral medicine that inhibits the multiplication of viruses which genetic material is RNA

RNA: ribonucleic acid, the second type of nucleic acid after DNA, also carrying genetic information. In humans, it plays a 'helper' role for DNA but is the only genetic material for some viruses.

SARSTer: a project investigating the effectiveness of various types of COVID-19 therapies used in Poland, implemented by the Polish Society of Epidemiologists and Doctors of Infectious Diseases

Protective vaccination: administration of an infectious disease vaccine for the purpose of artificial immunization against this disease

Oxygen therapy: a treatment method that consists of increasing the concentration of oxygen in the inhaled air

Immune system: is responsible for how the immune mechanisms work in the body

Virus (Latin: virus, poison): particles containing only one type of DNA or RNA nucleic acid that reproduce by infecting living cells

Cold chain: all activities aimed at the maintenance and monitoring of storage, transport, and distribution conditions in order to maintain the durability and effectiveness of the product



Resources:

Medical rationale for vaccinations:

1. The National Institute of Public Health-National Institute of Hygiene. All about vaccinations: <https://szczepienia.pzh.gov.pl/wszystko-o-szczepieniach/>
2. Vaccination against COVID-19: <https://www.gov.pl/web/szczepimysie>
3. Position of the Expert Group for COVID-19 of the Polish Academy of Sciences: <https://www.gov.pl/web/nauka/szczepienie-jest-jedynym-racjonalnym-wyborem-dzieki-ktoremu-bedziemy-mogli-szybciej-wyjsc-z-pandemii--stanowisko-zespołu-ds-covid-19>
4. World Health Organization. Coronavirus disease (COVID-19): Vaccines. [https://www.who.int/news-room/q-a-detail/coronavirus-disease-\(covid-19\)-vaccines](https://www.who.int/news-room/q-a-detail/coronavirus-disease-(covid-19)-vaccines)

mRNA technology and its application in vaccination:

1. Centers for Disease Control and Prevention. Understanding mRNA COVID-19 vaccines: <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/mrna.html>
2. Pardi N, Hogan MJ, Porter FW, Weissman D. Vaccines mRNA – a New Era in Vaccinology. Nature Reviews. Drug Discovery. 2018; 17 (4): 261-279.
3. Maruggi G, Zhang C, Li J, Ulmer JB, Yu D. mRNA as a Transformative Technology for Vaccine Development to Control Infectious Diseases. Molecular Therapy. 2019; 27 (4): 757-72.
4. Jackson NAC, Kester KE, Casimiro D, Gurunathan S, DeRosa F. The Promise of mRNA Vaccines: A Biotech and Industrial Perspective. Npj Vaccines. 2020; 5 (1): 1-6.

SARS-CoV-2 as the cause of the global pandemic:

1. Coronavirus infection report (SARS-CoV-2): <https://www.gov.pl/web/koronawirus/mapa-zarazen-koronawirusem-sars-cov-2-powiaty>
2. World Health Organization. Coronavirus: https://www.who.int/health-topics/coronavirus#tab=tab_1
3. Cascella M, Riarka M, Cuomo A, Dulebohn SC, Di Napoli R. Features, Evaluation, and Treatment of Coronavirus. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 October 4.

Registration and marketing authorization of medicinal products with regard to SARS-CoV-2 vaccines:

1. European Medicines Agency. Treatments and vaccines for COVID-19. <https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines-covid-19>
2. European Medicines Agency. COVID-19 vaccines: key facts. <https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/covid-19-vaccines-key-facts>
3. European Council. COVID-19 vaccines: Why so fast? <https://newsroom.consilium.europa.eu/events/20201210-european-council-december-2020-day-1/129127-covid-19-vaccines-why-so-fast-20201209>
4. The Act of December 5, 2008, on preventing and combating infections and infectious diseases in humans, Journal of Laws of 2008 No. 234, item 1570.

Clinical trials of SARS-CoV-2 vaccines:

1. Jackson LA, Anderson EJ, Routhae NG, Roberts PC, Makhene M, et al. An mRNA Vaccine against SARS-CoV-2 – Preliminary Report. N Engl J Med. 2020; 383 (20): 1920-1931.
2. Mulligan MJ, Lyke KE, Kitchin N, Absalon J, Gurtman A, et al. Phase I / II study of COVID-19 RNA vaccine BNT162b1 in adults. Nature. 2020; 586 (7830): 589-593.
3. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020; doi: 10.1056 / NEJMoa2034577.
4. Voysey M, Costa Clemens SA, Madhi SA, Weckx LY, Folegatti PM, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomized controlled trials in Brazil, South Africa, and the UK. Lancet. 2020; S0140-6736 (20): 32661-1

Selected documents of foreign competent authorities or public health authorities regarding SARS-CoV-2 vaccines:

1. Food and Drug Administration. Vaccines and Related Biological Products Advisory Committee Meeting. FDA Briefing Document. Moderna COVID-19 Vaccine. December 17, 2020. <https://www.fda.gov/media/144434/download>
2. Food and Drug Administration. Vaccines and Related Biological Products Advisory Committee Briefing Document. PFIZER-BIONTECH COVID-19 VACCINE (BNT162, PF-07302048). December 10, 2020. <https://www.fda.gov/media/144246/download>
3. Public Health England. COVID-19: the green book, chapter 14a. December 2020. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/943663/Greenbook_chapter_14a_v3.pdf

Immunization Plan and Importance of Primary Care Physicians and Nurses:

1. Free Hotline of the National Immunization Program against COVID-19, tel. 989 or (22) 62 62 989, video chat at gov.pl/szczepimysie (from 8 am to 4 pm on working days)
2. National Immunization Program against COVID-19. <https://www.gov.pl/web/szczepimysie/narodowy-program-szczepien-przeciw-covid-19>
3. COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE EUROPEAN COUNCIL, THE COUNCIL AND THE EUROPEAN INVESTMENT BANK. EU strategy for vaccines against COVID-19. Brussels, 17/06/2020 <https://eur-lex.europa.eu/legal-content/PL/TXT/PDF/?uri=CELEX:52020DC0245&from=PL>
4. European Commission. Coronavirus vaccination strategy. https://ec.europa.eu/info/live-work-travel-eu/coronavirus-response/public-health/coronavirus-vaccines-strategy_pl





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