

Opinion of BAS on the forthcoming vaccination campaign against COVID-19 (December 21, 2020)

The Bulgarian Academy of Sciences (BAS) has amongst its members some of the most prominent Bulgarian clinicians, biologists, immunologists, virologists, geneticists, mathematicians and other diverse specialists who are engaged with the global pandemic caused by the new coronavirus. Through their research work and active participation in various media presentations, where they share the most up-to-date and objective data on the pandemic, they contribute a lot to public awareness and to directing the fight against coronavirus in a scientifically sound way. In view of all this, we consider it necessary to express our opinion on the forthcoming vaccination campaign against coronavirus infection, taking into account the analysis of the existing data from the world literature and current practices.

Without dwelling on the very complex medical and economic issues related to the growing pandemic and the efforts to control it in our country and around the world, we would like to present information briefly, especially on issues related to available vaccines, their importance and the way the immunization program is organized in our country. We believe that this will help in properly understanding the great importance of immunization and will help to alleviate public anxiety about false, unscientific or contradictory information that is circulating.

In the absence of a specific and effective drug against coronavirus infection, which modern medicine does not yet have, apart from strict adherence to anti-epidemic measures, the only option is a vaccine. This is proven by the vast experience that humanity has gained in the fight against infectious diseases throughout the ages. A vaccine that is harmless and has an effectiveness of at least 50-60% (i.e. creates immunity in such a percentage of those immunized) will play a huge role in limiting infection. Unfortunately, the data we have so far show that collective immunity to coronavirus is very slow and practically difficult to achieve naturally (which is also associated with major ethical and moral challenges), so vaccines will help a lot in achieving it.

To date, more than 220 coronavirus vaccines are being developed worldwide, of which 56 are in clinical trials and more than 10 are in the third (most important) phase of a clinical trial, which requires, according to globally accepted rules, administering them to 30,000 - 40,000 people to objectively assess their safety and effectiveness. It should be well known that under normal conditions a vaccine is developed in 3-5 years or more. But the situation in which the whole world finds itself - a very severe and rapidly spreading infection that takes hundreds of thousands of lives and is a colossal health, social and economic problem, justifies the permission by the WHO, the international and national regulators and government agencies to accelerate the introduction of vaccines, in accordance with all requirements for well-proven safety. No compromise is made in this regard and vaccines must meet well-established high world standards and the expected benefits of their use should far outweigh the foreseeable potential risks. As for the effectiveness of vaccines and the nature of the immunity they create and its duration, we will be able to give a satisfactory answer not earlier than one year from the beginning of their application, when we will have sufficient convincing scientific data as a result of monitoring hundreds of thousands immunized. In essence, this is the so-called fourth or 'post-marketing' phase of the clinical trial.

We will outline the main approaches for the development of anti-covid-19 virus vaccines:

- *RNA vaccines.* On a pre-prepared (synthetic) mRNA platform, which is loaded with genetic material from the coronavirus and included in liposomes (for greater stability and antigenicity), the synthesis of viral antigen is stimulated in the human body, which subsequently causes the synthesis of protective viral antibodies and cellular immunity. The vaccines of the companies Pfizer and BioNTech and Moderna were created on this most modern principle. Their studies showed that mRNA does not damage the human genome or interact with DNA. In addition, it decomposes very quickly and does not circulate in the body.
- *Vector vaccines.* A harmless human adenovirus (or other viruses) that is loaded with SARS-Cov-2 genetic material is used as a vector in immunization. This is how the vaccines of Astra Zeneka, Janssen-Cilag, the Russian vaccines Sputnik and Vector and others were developed.
- *Protein vaccines.* Protein components from the ‘spikes’ of the virus, from its shell or body (nucleocapsid), which have proven antigenic (immunostimulatory) activity are used (Sanofi-GSK).
- *Adjuvant vaccines.* An attenuated SARS-Cov-2 virus is used for immunization. Very often in combination with the so-called adjuvant (enhancer) of the immune response. This is how some Chinese and Cuban vaccines were created.

All of these vaccines require two doses to be administered, the second dose being administered 21 to 28 days after the first. According to the data presented by the various manufacturers, resulting from the clinical study, they do not cause serious side effects and sufficiently stimulate humoral (antibody) and cellular immunity.

In the European Union (EU) so far (18 December 2020) 5 vaccines have been presented for registration by the European Medical Agency (EMA): Pfizer / BioNtech, Moderna, Astra Zeneka, Janssen-Cilag and Sanofi-GSK, with several more ready to be presented. The final decision on their approval will be taken on December 21, 2020, after which it will be possible to roll them out in the EU. The Pfizer / BioNtech vaccine was approved by the UK regulators a few days ago and approved for use in the UK. Immunization with the Russian Sputnik V vaccine has been carried out for 1-2 months on certain contingents in the Russian Federation, and the same is happening in China, where immunization is carried out with two different Chinese vaccines approved by the regulatory authorities of Russia and China respectively. Immunization with the FDA-approved vaccine Moderna in the United States has been underway for several days.

According to the general EU action plan against the COVID-19 pandemic, Bulgaria will first import the Pfizer / BioNtech vaccine within a few days and will start its roll out after the expected EMA approval. The vaccine will be free and voluntary. To this end, a very active organization has been launched to solve important logistical problems related to the application of the vaccine: ensuring its proper storage and transport, as this requires strict adherence to refrigeration temperatures from -70 ° C to -80 ° C; establishing an appropriate organization for immunization; determining the places for its implementation and the persons who will be in charge of it; most importantly - determining the contingents to be immunized and the ways to inform and attract them; conducting a broad awareness campaign on the importance of vaccines for both individuals and the public health in order to boost collective immunity and limit the spread of infection. In this

regard, the Ministry of Health has created a detailed work plan, the implementation of which has begun. All this is forthcoming and will develop very dynamically, in view of the rapidly changing situation with the coronavirus pandemic in our country and around the world, and will depend on the approval of other vaccines and their importation. This will probably set new requirements in the course of immunization and the way it is carried out.

In conclusion, we allow ourselves to say that it is recommended that all healthy people, without accompanying severe chronic diseases, without clinical manifestations at the moment and over 16-18 years of age be immunized. It is mandatory to first contact their general practitioner (GP) to discuss this issue, taking into account all the indications and contraindications for vaccination, described in detail in the so-called 'brief description', or its 'passport'. This implies the rapid organization of a broad media and institutional campaign so that doctors and citizens can be very well informed and convinced of their decision which is of great personal and public interest.