Anti-COVID-19 vaccination with mRNA vaccines

To date, two anti-COVID-19 vaccines have been approved by the European Medicines Agency and AIFA: COVID-19 Pfizer mRNABNT162b2 vaccine (Comirnaty) and Moderna mRNA -1273 vaccine.

CHARACTERISTICS AND SAFETY of the Pfizer mRNABNT162b2 vaccine (Comirnaty)

1. What is it and what is it used for?

COVID-19 mRNA BNT162b2 vaccine (Comirnaty) is a vaccine indicated for preventing the 2019 coronavirus disease (COVID-19) in people aged 16 years and older. It contains a molecule called messenger RNA (mRNA) provided with the instructions for producing a protein present on SARS-CoV-2, the virus responsible for COVID-19 disease. The vaccine does not contain the virus itself and cannot cause the disease.

2. How is it administered?

COVID-19 mRNA BNT162b2 vaccine (Comirnaty) is given in two injections, usually into the deltoid muscle of the upper arm, at least 21 days apart.

3. What does it contain?

COVID-19 mRNA BNT162b2 vaccine (Comirnaty) contains a messenger RNA that cannot reproduce itself in host cells, but prompts the synthesis of antigens of the SARS-CoV-2 virus (that the virus itself encodes). The S antigens of the virus stimulate the antibody response of the vaccinated person through production of neutralizing antibodies.
The messenger RNA is enclosed in liposomes formed by ALC-0315 and ALC-0159 to facilitate entry into cells.
The vaccine also contains other excipients:
1,2-Distearoyl-sn-glycero-3-phosphocholine, cholesterol, dibasic sodium phosphate dihydrate, monobasic potassium phosphate, potassium chloride, sodium chloride, saccharose, water for injections.

4. What is the dose to be injected and how many doses can be obtained per vial?

The dose of vaccine to be administered to each person is 0.3 ml. This dose should be withdrawn, under aseptic conditions and using appropriate precision syringes, from a vial of vaccine containing 2.25 ml after dilution with a 0.9% sodium chloride solution.
With an aim to use all the product available in each vial and to avoid any waste, AIFA, in accordance with the provisions of its Scientific-Technical Committee, states that, without prejudice to the need to guarantee the administration of the appropriate 0.3 ml dose to each vaccinated subject by using suitable syringes, it is possible to have at least 1 additional dose compared to the 5 doses declared in the Summary of Product Characteristics (SmPC).

Any residues from different vials, even those belonging to the same batch number, shall not be mixed.

5. How were clinical trials conducted?

A very large clinical trial showed that COVID-19 mRNA BNT162b2 vaccine (Comirnaty) is effective in preventing COVID-19 in people from 16 years of age.

The efficacy and safety profile of this vaccine was assessed in trials across six countries (USA, Germany, Brazil, Argentina, South Africa and Turkey), involving more than 44,000 participants.

Half received the vaccine and half were given a placebo, a product identical to the vaccine but inactive. Efficacy was calculated over 36,000 people aged 16 years and older (including people over 75 years of age) who had no sign of previous infection.

The study showed a 95% reduction in the number of symptomatic COVID-19 cases in the subjects who received the vaccine (8 cases out of 18,198 had COVID-19 symptoms) compared with the subjects who received a placebo (162 cases out of 18,325 had COVID-19 symptoms).

6. How effective is it?

Trial findings showed that two doses of COVID-19 mRNA BNT162b2 vaccine (Comirnaty) administered 21 days apart can prevent 95% of adults aged 16 years and older from developing COVID-19. Such findings were maintained across age brackets, genders and ethnic groups.

The 95% reduction refers to the difference between the 162 cases reported in the group of over 18,000 people who received a placebo and the only 8 cases reported in the group of over 18,000 people who received the vaccine.

7. Is protection effective right after the injection?

No, effectiveness has been proven one week after injecting the second dose.

8. What adverse reactions were observed?

The most frequent adverse reactions (affecting more than 1 in 10 people) observed in the COVID-19 mRNA BNT162b2 vaccine (Comirnaty) trial were usually mild or moderate and resolved within a few days after vaccination. These included pain and swelling at the injection site, fatigue, headache, muscle and joint pain, chills and fever.

Redness at the injection site and nausea occurred in less than 1 in 10 people. Itching at the injection site, limb pain, enlarged lymph nodes, difficulty in falling asleep and malaise were uncommon adverse reactions (affecting less than 1 in 100 people). Muscle weakness on one side of the face (acute peripheral facial paralysis or palsy) occurred rarely, in less than 1 in 1,000 people.

9. What serious adverse reactions were observed during the trial?

The most common serious adverse reaction occurring in both the vaccine and the placebo group was the enlargement of lymph nodes. However, this is a benign condition which resolves naturally. Overall, systemic reactions were more frequent and pronounced after the second dose.

Reports of adverse reactions, from the least serious to the most severe, including allergic reactions, are being collected in countries where mass administration of the vaccine has already started. All countries administering the vaccine to the entire population are collecting and assessing any adverse reaction reported to the relevant pharmacovigilance system in order to define the risk profile of the vaccination. For further information please refer to FAQs on pharmacovigilance.

CHARACTERISTICS AND SAFETY of the Covid-19 Moderna mRNA -1273 vaccine

1. What is it and what is it used for?

COVID-19 Moderna mRNA -1273 vaccine is a vaccine indicated for preventing the 2019 coronavirus diesase (COVID-19) in people aged 18 and older. It is the second anti-COVID-19 vaccine authorised in Italy by AIFA (on 7 January 2021), after the Comirnaty vaccine. It contains a molecule called messenger RNA (mRNA) provided with the instructions for producing a protein present on SARS-CoV-2, the virus responsible for COVID-19 disease. The vaccine does not contain the virus itself and cannot cause the disease.

2. How is it administered?

The vaccine is given in two injections, of 0.5 ml each, usually into the deltoid muscle of the upper arm, at least 28 days apart.

3. What does it contain?

COVID-19 Moderna mRNA -1273 vaccine contains a messenger RNA that cannot reproduce itself in host cells, but prompts the synthesis of the Spike (S) protein of the SARS-CoV-2 virus. The viral S protein stimulates the antibody response of the vaccinated person through production of antibodies neutralizing the virus, should one come into contact with the virus. To facilitate entry into cells, the vaccine mRNA is enclosed in very small vesicles (liposomes). In addition to mRNA, the vaccine also contains: SM-102, DSPC, PEG2000 DMG, potassium chloride, potassium dihydrogen phosphate, sodium chloride, disodium phosphate dihydrate, saccharose, water for injections.

4. What are the storage and administration characteristics?

The vaccine is stored at temperatures between -15°C and -25°C, but is stable between +2°C and +8°C for 30 days if the package remains intact. The multidose vial contains 6.3 ml and does not require dilution; it is therefore ready for use and allows the administration of 10 doses, although in many cases it may be possible to obtain a complete eleventh dose of 0.5 ml. Any residues from different vials, even belonging to the same batch number, shall never be mixed.

5. How were clinical trials conducted?

A very large clinical trial proved that COVID-19 Moderna vaccine is effective in preventing COVID-19 disease in subjects aged 18 onwards. The efficacy and safety profile of this vaccine was assessed in trials conducted by 99 centres in the United States, which involved 30,420 participants from 18 years onwards.

The participants were divided into two groups: 15,210 received the vaccine and the same number were given a placebo, a product identical in all respects to the vaccine, but not active. More than half (58.6%) of the participants were aged between 18 and 64, 24.8% were 65 or older and 16.7% were younger than 65 but with concomitant diseases which increased the risk of severe COVID-19 disease. 47.3% were women. Overall, 11 cases of COVID-19 disease were recorded in the group that received the vaccine, compared to 185 in the group that received the placebo and acted as control: therefore, the vaccine showed a 94.1% efficacy in preventing infection with SARS-CoV-2 symptoms versus placebo.

6. How effective is it?

The results of these studies showed that two doses of the Moderna vaccine, administered 28 days apart, were able to prevent 94.1% of vaccinated adults aged 18 and over from developing the COVID-19 disease referred to 11 cases among the vaccinated group and 185 cases in the placebo group; the results were substantially homogeneous by age, gender and ethnicity. All severe cases of COVID-19 (30 in total, with 1 death) occurred to the study participants, were recorded in the control group. Such results confirm that the vaccine is able to prevent the severe form of the disease caused by the SARS-CoV-2 virus.

7. Is protection effective right after the injection?

No, effectiveness was completed two weeks after injecting the second dose.

8. What adverse reactions were observed?

The most common adverse reactions were pain at injection site (92%), fatigue (70%), headache (64.7%), muscle pain (61.5%), chills (45.4%), nausea/vomiting (23%), swollen lymph nodes in the arm of injection (19.8%), fever (15.5%), swelling (14.7%) and redness (10%) at the injection site. Reactions were generally mild or moderate in intensity and resolved within a few days from vaccination. Reactions were more frequent after the second dose and in younger participants aged between 18 and 65 years, compared to participants over 65 years.

9. What serious adverse reactions were observed during the trial?

The frequency of more severe adverse events was comparable between the control group (1.3%) and the group receiving the vaccine (1.5%). In less than 0.5% of cases, in both groups, adverse events were such as to prevent administration of the second dose. No cases of respiratory diseases associated with the vaccine were reported. For further details, please refer to FAQs on pharmacovigilance.

MECHANISMS OF ACTION AND PROTECTION of Pfizer and Moderna vaccines

1. How do mRNA vaccines work?

SARS-CoV-2 viruses infect the body by using a surface protein, called Spike, that allows the viruses to penetrate into the body cells and reproduce themselves.

Vaccines currently being studied have been developed to prompt a response blocking the spike protein, thus preventing cell infection.

The two anti-COVID-19 mRNA vaccines approved for the vaccination campaign use messenger RNA (mRNA) containing instructions for the vaccinee's cells to synthesize Spike proteins. In vaccines, the mRNA molecules are inserted into microscopic lipid vesicles which allow the mRNA to enter the cells. Once injected, the mRNA is absorbed into the cell cytoplasm and initiates the synthesis of Spike proteins. Such proteins stimulate the immune system to produce specific antibodies. In those who have been vaccinated and are exposed to viral infection, the antibodies produced will block the Spike proteins and prevent their entry into the cells. In addition, vaccination also activates T cells that prepare the immune system to respond to further exposure to SARS-CoV-2. Therefore, the vaccine does not introduce the actual virus into the vaccinee’s cells, but only the genetic information required by the cell to build copies of the Spike protein. If, at a later time, the vaccinated persons come into contact with SARS-CoV-2 again, their immune system will recognize the virus and be ready to fight it. The vaccine mRNA does not remain in the body, but will degrade shortly after vaccination.

2. How long does vaccine protection last?

It is not currently known how long protection provided by the vaccine lasts, since the observation period was inevitably limited to few months. However, evidence from other coronavirus strains shows that protection should be at least 9-12 months.

3. Can mRNA vaccines cause COVID-19 disease or other genetic modifications?

These vaccines do not use active viruses, but only a genetic component carrying into the vaccinee's body the instructions to produce specific antibodies. Whole or live viruses are not involved, so the vaccine cannot cause diseases. As any mRNAs produced by cells, the vaccine mRNA naturally degrades a few days after vaccination.

4. Can vaccinated persons spread the infection to others?

Clinical studies conducted so far have assessed the efficacy of mRNA vaccines on clinically manifest forms of COVID-19. However, more time is needed to obtain significant evidence as to whether vaccinated people can become asymptomatically infected and then infect other people. Although vaccination is likely to protect against infection, vaccinated persons and those with whom they come into contact should continue to take protective measures against COVID-19

5. Has the clinical trial duration been shortened to obtain such vaccines sooner?

Studies on anti-COVID-19 vaccines, including mRNA vaccines, began in spring 2020. Therefore, they lasted only a few months compared to usual times, but saw the participation of a very large number of people, ten times higher than usual vaccine development studies. Therefore, it was possible to carry out a sufficiently large study to demonstrate the vaccine efficacy and safety.

None of the regular phases for the verification of the vaccine's efficacy and safety was skipped: the short timelines leading to the swift approval were possible thanks to the research already carried out for many years on RNA vaccines, to the great human and financial resources made available in a very short time and to the assessment, by the regulatory agencies, of the results obtained as they became available and not, as usually happens, when all studies were completed. These simple measures saved years on approval times.

6. Do the vaccines protect only the vaccinated persons or their family too?

The vaccines protect the individual, but if many people get vaccinated, the spread of the virus can be reduced to some extent, which will in turn protect all those who cannot be vaccinated. Vaccination helps to protect both the individual and the general population.

7. Does vaccination allow you to go back to life as it was before?

Although the effectiveness of the vaccines available is very high (over 90%), there will always be a share of vaccinated people who does not develop an immune response. Moreover, it is still not known whether vaccination prevents just the expression of the disease or the spreading of the infection as well. This is why being vaccinated does not give a "go-ahead", but it is necessary to continue to adopt correct behaviours and measures to contain the infection risk.

8. A new SARS-CoV-2 virus variant has been detected. Will the vaccines be effective also against it?

RNA viruses, such as SARS-CoV-2, are subject to frequent mutations, most of which do not significantly alter the virus structure and components. Many variants of SARS-CoV-2 were reported in 2020, but so far these variants have not altered the natural behaviour of the virus.

The variant reported in the UK is the result of a series of surface protein mutations, and assessments are being carried out of the effects that these may have on the course of the epidemic. A negative effect on vaccination is unlikely.

9. Why not adopt the British strategy of immediately administering the first dose to as many people as possible and delaying the second dose?

Published studies show that one dose is sufficient to prompt the desired immune response within two weeks and that such response is strongly enhanced by the second dose. We do not know how long immunity lasts after the first dose. A population vaccinated with a single dose has its risk of getting COVID-19 only halved. The Center for Disease Control in the United States stated that for both mRNA vaccines (Pfizer/BioNTech and Moderna) "the second dose should be given as close as possible to the recommended interval", which is 21 days and 28 days respectively. A similar indication was given by the World Health Organization. Therefore, AIFA's Scientific Committee on Vaccines deems it necessary to follow the current indications on the administration of two doses for the vaccines approved so far.

WHAT ARE THE DIFFERENCES BETWEEN THE TWO VACCINES?

The two vaccines are very similar and have been evaluated as equivalent by AIFA's Scientific-Technical Committee, in that they adopt the same messenger RNA technology, have a very high efficacy (almost equal), they are both very safe, with modest side effects and largely resolved in a few days. Both vaccines deliver a massive immune response after two doses three to four weeks apart. They have been studied on tens of thousands of participants with the most rigorous scientific methods. Comirnaty shows efficacy data from 16 years of age onwards, Moderna from 18 years onwards.

The differences are also in the way they are presented: frozen Comirnaty to be diluted and Moderna ready and kept at refrigerator temperatures.

A synoptic comparison table between the two vaccines is available here.

CONDITIONS FOR VACCINATION of the Pfizer and Moderna vaccines

1. Can/Must people who have already had confirmed COVID-19 be vaccinated?

Vaccination does not conflict with a previous COVID-19 infection. It actually enhances immunological memory; therefore, no tests are necessary before vaccination. However, people who have been diagnosed COVID-19-positive do not need vaccination in the first phase of the vaccination campaign. Vaccination may be considered when data on the duration of immune protection are available. In any case, it is not necessary to undergo diagnostic tests for Covid-19 before vaccination.

2. Can people with chronic diseases, diabetes, cancers and cardiovascular diseases be vaccinated?

Since these people are most at risk of developing a serious condition in case of SARS-CoV-2 infection, they will be given priority for receiving the vaccine.

3. Can people who have recently received the influenza vaccine be vaccinated against COVID-19?

There are still no data on the interference between COVID-19 vaccinations and other vaccinations. However, the nature of mRNA vaccines suggests that it is unlikely for this vaccine to interfere with other vaccines. However, a two-week interval shall be observed as a precautionary measure.

4. Can pregnant or breast-feeding women be vaccinated?

Data on the use of these vaccines during pregnancy and lactation are still very limited, however laboratory studies on animal models have not shown harmful effects. In particular, the vaccines are not contraindicated and do not exclude *a priori* pregnant women from vaccination, in that pregnancy, especially if combined with other risk factors such as diabetes, cardiovascular disease and obesity, could make them more exposed to risk in case of severe COVID-19 disease. As for breastfeeding, despite the lack of specific studies, there is no biologically plausible risk preventing them from continuing breastfeeding. The Italian National Health Institute (*Istituto Superiore di Sanità*), through the *ItOSS* project, is participating in the national and international debate on these aspects and has recently published a document with the aim of supporting healthcare professionals, pregnant and breastfeeding women in the decision-making process regarding vaccination. As a general rule, vaccination during pregnancy and breastfeeding should be decided in close consultation with a healthcare professional, after balancing risks and benefits.

5. Can children be vaccinated with the COVID-19 mRNA vaccines?

Both vaccines are not currently recommended for children below 16 years (Comirnaty) and 18 years (Moderna). The European Medicines Agency (EMA) has agreed with the company manufacturing Comirnaty on a plan to trial the vaccine in children at a later stage.

6. Can people with respiratory allergies (rhinitis, conjunctivitis, bronchial asthma) be vaccinated with mRNA vaccines?

People who suffer or have suffered from respiratory allergy can be vaccinated, remaining under observation, like everyone, for 15 minutes after the injection. Any ongoing antiallergic treatment, including specific immunotherapy, shall not be suspended.

7. Can people with severe persistent bronchial asthma be vaccinated?

For those suffering from severe persistent bronchial asthma, vaccination is recommended under medical supervision in a protected environment (hospital). In the case of uncontrolled asthma, the administration of the vaccine should be postponed until the clinical situation is again under control.

8. Can people with food allergies be vaccinated?

People with food allergies can be vaccinated by remaining under observation, like everyone, for 15 minutes after the injection. Should you have previously experienced severe allergic reactions (anaphylaxis) to food, you shall remain under medical supervision for 60 minutes. If severe persistent bronchial asthma is associated with food allergy, vaccination should be performed in a protected environment (hospital).

9. Le persone con allergie a farmaci o ai loro eccipienti possono vaccinarsi?

People with drug allergies can be vaccinated remaining under observation, like everyone else, for 15 minutes after the injection. Should you have previously experienced severe allergic reactions

(anaphylaxis) to medicines, you shall must remain under medical supervision for at least 60 minutes. If severe persistent bronchial asthma is associated with drug allergy, vaccination should be performed in a protected environment (hospital). People with allergy to polyethylene glycol (PEG), macrogol and polysorbate excipients, should not receive mRNA vaccines.

10. Can people with contact allergies (dermatitis) be vaccinated?

People having previously experienced contact dermatitis can be vaccinated, remaining under observation, like everyone, for 15 minutes after the injection.

11. Can people who have experienced a severe allergic or non-allergic adverse reaction to the first administration of Covid-19 vaccine receive the second dose?

No, people having previously experienced severe, allergic and non-allergic reactions, to the first dose, should not be administered the second dose, but should contact a referral centre with experience on reactions to vaccinations, to receive specialist information.

12. Can people with mastocytosis be vaccinated?

For vaccination of people with mastocytosis it is recommended, as with routine vaccines, oral anti-histamine coverage from 1 day before to 5 days after vaccination, and to remain under medical supervision for at least 30 minutes after the injection. In case of previous anaphylactic reactions to any substance, the supervision period should be extended to 60 minutes.

13. Can people with celiac disease or organ-specific autoimmune diseases (e.g., Hashimoto's thyroiditis) be vaccinated?

People suffering from celiac disease or organ-specific autoimmune diseases can be vaccinated, as these diseases are not a contraindication to vaccination.

14. Can people on anticoagulant therapy be vaccinated?

People on anticoagulant therapy can be vaccinated without stopping their ongoing treatment. Vaccination shall be carried out before taking the therapy. For intramuscular injection, the use of a fine needle (less than or equal to 23 gauge) is recommended and compression shall be performed on the injection site for 5 minutes. A check of the injection area is recommended after 2-4 hours to detect the possible occurrence of any hematoma.

15. Can people with coagulation disorders be vaccinated?

People with coagulation disorders (e.g., haemophilia, Von Willebrand's disease) should be carefully assessed before administering intramuscular vaccines against the risk of bleeding. Whenever possible, disease control should be optimized prior to vaccination. In patients on replacement therapy, vaccination should be scheduled shortly after therapy administration. For intramuscular injection, the use of a fine needle (25-27 gauge) is recommended and compression shall be performed on the injection site for at least 10 minutes. A check of the injection area is recommended after 2-4 hours to detect the possible occurrence of any hematoma.

16. Can people with documented immunodeficiency or autoimmune diseases be vaccinated?

No data are yet available on the safety and efficacy of mRNA vaccines in people suffering from autoimmune diseases, which were however included in the initial trials. During clinical trials, no differences were observed in the appearance of symptoms attributable to autoimmune or inflammatory diseases between vaccinated and placebo-treated subjects. People with autoimmune diseases who have no contraindications can receive the vaccine. The data relating to

use in immunocompromised people (i.e., whose immune system is weakened) are limited in number. While these people may not respond as well to the vaccine, there are no particular safety concerns. Immunocompromised people can be vaccinated in that they may be at high risk for COVID-19.

17. Should people who become infected with COVID-19 after being administered the first dose of the vaccine receive the second dose?

In the majority of the population, the first dose of the vaccine prompts an initial immune response providing only partial protection. Depending on the type of vaccine, protection starts after about 2-3 weeks from the first dose, thus keeping the risk of COVID-19 still consistent, albeit reduced.
The second dose of vaccine is therefore required to increase the immune response and obtain optimal vaccine protection.
In the case of people with SARS-CoV-2 infection/disease confirmed by a third generation molecular or antigen test after the first dose of the vaccine, the infection itself represents a powerful stimulus for the immune system, which adds to the one provided by the first dose of vaccine.
In light of this and considering that natural infection initiates a specific immune response to the virus, it is not recommended to administer the second vaccination dose to these people. Partial vaccination and subsequent infection do not preclude a possible booster dose of COVID-19 vaccination in the future, if data on duration of immune protection indicate such need.

VACCINATION PROCEDURES of the Pfizer and Moderna vaccines

1. Who will administer the vaccine?

Vaccination shall be performed by healthcare professionals of public vaccination centres, i.e., people with extensive vaccination experience and trained in vaccination techniques. Furthermore, considering the specific features of these vaccines, healthcare professionals have received additional specific technical information on the preparation and administration of the vaccines.

2. How is the absence of contraindications guaranteed?

Before vaccination, healthcare professionals will ask the person who is going to receive the vaccine a series of precise and simple questions, using a standardised form. Based on the answers given by the person, healthcare professionals will consider whether vaccination should be carried out or postponed. In addition, healthcare professionals shall verify whether there are contraindications or special precautions need to be taken, as reported in the vaccine data sheet.

3. Can people who receive the first dose of a COVID-19 mRNA vaccine complete the vaccination course with a second dose of the other vaccine?

There are no data available on the interchangeability between different COVID-19 vaccines to complete the vaccination course, therefore people who have received one dose of COVID-19 mRNA vaccine should receive a second dose of the same vaccine.

4. Who shall I contact to be vaccinated?

The vaccination campaign will be carried out at subsequent phases, with citizens being invited to get vaccinated according to an order of priority defined by the risk for people to be infected and develop the disease with serious consequences, the social function of some professional

categories (teachers, police forces); then the elderly (over 65 years) and finally the remaining population.
In the initial phase, priority will be given to healthcare professionals as well as staff and guests of retirement homes; vaccinations will be carried out by vaccination centre staff in the 286 hospitals identified by the National COVID-19 Vaccination Plan. The same vaccination staff will provide vaccination at retirement homes.

5. How much does the vaccination cost?
The vaccination is free for everyone.

6. Is it possible to get vaccinated privately for a fee?
No, currently available vaccines will only be used in the facilities identified by the Vaccination Plan and will not be available in pharmacies or on the private market. People are highly discouraged to try to obtain the vaccine through alternative channels or on the Internet. These channels give no guarantee on the quality of the product, which could be harmful for health as well as ineffective.

7. How does the injection procedure work?
During the handling of the vaccine and the injection, as with any intramuscular injection, there is a risk of contamination of the needles and syringes used due to environmental germs which, in case of incorrect procedure, could be injected together with the vaccine. If this happens, inflammation of the injection site of varying intensity may occur, up to purulent abscess. To avoid this risk, aseptic techniques must be adopted, in particular, through minimizing environmental exposure of the syringe needles and bevel. The procedure for the Pfizer vaccine requires the use of a 3ml syringe to withdraw the dilution liquid to be injected into the multidose vial. Then, after dilution, withdrawal of 0.3 ml of vaccine and injection for a total of six doses. This procedure is feasible with normal 3- or 5-ml standard syringes, for dilution, and 1 ml syringes (insulin type) for injection, whereas the Moderna vaccine comes in ready-made vials of 6.3 ml from which it is possible to withdraw up to eleven doses of 0.5 ml of vaccine.

8. What is the syringe Luer lock system?
The Luer lock system provides for the permanent connection of the needle to the syringe, not allowing any separation for both the 3 ml and 1 ml syringes. The needles also have the same connection. This system guarantees against:

1. The accidental separation of the needle from the 3 ml syringe during withdrawal and injection into the vial, as well as against separation of the needle from the syringe for the withdrawal and injection of the 0.3 ml of vaccine;

2. The reckless practice of leaving a needle stuck in the diluted vaccine vial to subsequently withdraw the 6 doses and inject them with different needles;

3. The reckless practice of withdrawing multiple doses of dilution (e.g., 2*1.8 = 3.6ml) using the same syringe for multiple vaccine vials;

4. The even more dangerous practice of withdrawing multiple doses of vaccine from the vaccine vial (e.g., 3*0.3 = 0.9 ml) by only changing the needle for multiple vaccinees.

Such practices are very dangerous due to exposure of needles and syringe bevels to microbial contamination and are already absolutely banned. However, in an extraordinary mass vaccination such as the one underway, errors cannot be ruled out, as already noted in some European countries. The Luer lock system adds to the connection through simple insertion of the needle to the syringe, which is common to normal syringes, a connection through screwing breading which welds the needle to the syringe, thus guaranteeing the prevention of the abovementioned errors, in that every needle and every syringe can be used only once.

9. What is the dead space of a syringe?

All syringes have a dead space: the small space between the plunger and the bottom of the syringe and the space inside the injecting needle. It is a variable amount of fractions of tenths of a milliliter. The liquid filling this space is actually lost and therefore slightly reduces the dose administered. The problem is irrelevant for quantities of drug measurable in milliliters (1.2-5.10ml), whereas it can be significant when the dose is smaller, like the 0.3 ml dose of the Pfizer vaccine and the 0.5 ml dose of the Moderna vaccine, especially if it is possible to exactly withdraw six or seven doses from the Pfizer vial or ten doses from the Moderna vial. For this reason, precision 1 ml insulin-like syringes should be preferred, with minimal or almost no dead space. The 1 ml Luer loch syringes have the advantage of both safety, as described in the previous answer, and optimization of dose withdrawal.

10. How to prevent risks for healthcare operators?

As any invasive health procedure, also vaccine injection shows a minimal risk due to handling of sharp objects such as needles: despite numerous national, European and WHO guidelines and regulations, the risk due to needle stick still displays significant numbers in Italy; therefore, it is deemed advisable to recall the Law Decree 19 February 2014 no. 19, providing regulations aimed at preventing these risks and namely Article 286 sexies, which expressly prohibits re-capping of the needle after injection, also providing for immediate disposal of the entire syringe, with the needle, in the special puncture-proof containers.

11. Will there be vaccines for everyone?

Through European procedures, the Italian government has booked the purchase of over two hundred million doses of COVID-19 vaccines from six different manufacturers. The person receiving the vaccine cannot freely choose which vaccine to receive: the vaccine available at the relevant time and place will be offered by the vaccination centres with a full guarantee of equivalent safety and efficacy.

12. Will only Italian citizens be vaccinated?

According to the priority scheme defined in the Vaccination Plan, all people will be vaccinated who are present on the Italian territory, residents with or without a residence permit pursuant to Article 35 of Consolidated Law on Immigration.

13. Which documents are required for vaccination?

A valid identity document and health card (*tessera sanitaria*) are required. It may be useful to show any health documentation helping the vaccinating healthcare professional to assess the person's physical condition.

14. Which documents are required for socially-vulnerable (Italian and foreign) people to receive the vaccine?

Based on Article 32 of the Italian Constitution and pursuant to the provisions of Article 35 of the Consolidated Law on Immigration, the required documents comprise any document (including expired ones) stating the identity of the person receiving the vaccine, the health card (tessera sanitaria), the European Health Insurance Card, the STP code (straniero temporaneamente presente – Temporarily present foreign person) and the ENI code (Europeo non iscritto – Non registered European citizen).

15. Who can I contact if I have a reaction after administration of the vaccine?

Like all adverse reactions to medicinal products, adverse reactions to the vaccine can be reported to general practitioners/family doctors and to local health authorities (ASL), in agreement with the pharmacovigilance system in place. Moreover, anyone can report an adverse reaction to the vaccine by using the forms published on the AIFA website. For further details, please refer to the pharmacovigilance section.

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