AGENZIA ITALIANA DEL FARMACO

COVID-19 vaccines
FAQ on pharmacovigilance

1. **What does pharmacovigilance mean?**
   Each medicinal product has benefits and risks which are carefully evaluated during the authorization procedures and continuously re-evaluated after being marketed. Pharmacovigilance is a series of activities which aim to continuously collect all safety data and information available on the use of medicinal products (drugs and vaccines). Such continuous evaluation ensures, among other things, that the benefit/risk ratio remains favourable over time, i.e., by guaranteeing that the health benefits outweigh any risks.
   Data and information on the safety of drugs and vaccines can be obtained from different sources, such as reports of suspected adverse reactions, clinical studies and scientific literature. In Italy, pharmacovigilance is one of the tasks of the Italian Medicines Agency (AIFA).

2. **Are adverse events, adverse reactions and undesirable effects the same thing?**
   An **adverse event** is any unfavourable episode occurring after the administration of a drug or vaccine, but which is not necessarily caused by taking the drug or by having received the vaccination.
   An **adverse reaction**, on the other hand, is a harmful and unintended response to a drug or vaccination for which a causal relationship with the drug or vaccination can be established. Therefore, to distinguish whether we are dealing with an adverse event or an adverse reaction, we should assess whether it is possible to trace a cause linked to the medicinal product: https://www.who.int/vaccine_safety/publications/gvs_aefi/en/.
   It is not sufficient that the event occurred shortly after vaccination or medicine administration.
   An **undesirable effect** is an unintended effect related to the properties of the drug or vaccine, which is not necessarily harmful and has been observed in a number of people. It is therefore a possible known effect, which has occurred over time and is considered acceptable.
3. **What is meant by "adverse event following vaccination"?**
   An Adverse Event Following Immunization (AEFI) is any adverse event of a medical nature that occurs *after* the administration of a vaccine (temporal relationship), but which is not necessarily *caused by* vaccination (causal relationship). Indeed, an event occurring *after* vaccination does not necessarily imply that it was caused by the vaccination itself. Many adverse events can only be coincidental or determined by other causes (known or unknown) prior to or concomitant with the vaccination itself. However, pharmacovigilance activities, especially in the initial studies, require that any adverse health events be reported within vaccinated people.

It has been observed that following the introduction of a new vaccine, reports of adverse events often increase, probably due to greater attention from both health professionals and citizens. Collecting and analyzing all these reports is useful to better understand the benefit/risk ratio of the vaccine.

The AEFI are divided into 5 categories:

a) Product-related reaction
b) Quality defect-related reaction
c) Immunization error-related reaction
d) Immunization anxiety-related reaction
e) Coincidental event

(https://vaccine-safety-training.org/classification-of-aefis.html)

4. **Why is any event occurring after vaccination considered an adverse event, even if a causal link is not demonstrated?**

Investigating *any* event occurring after a vaccination helps to gather as much information as possible and to increase the possibility of identifying truly suspicious events which are important to understand, or which have never been observed before, with the aim of ascertaining the presence of a causal link with vaccination.
In this way, regulatory authorities such as AIFA and EMA can verify the safety of vaccines in the real world, confirming what was observed in the studies prior to authorization and possibly identifying new potential adverse reactions, especially if rare (1 in 10,000) and very rare (less than 1 in 10,000).
Therefore, a large number of reports does not imply a greater danger of the vaccine, but is an indicator of the high ability of the pharmacovigilance system to monitor safety.

5. **How does the National Pharmacovigilance Network work?**

The National Pharmacovigilance Network is a system for collecting reports of suspected adverse reactions to drugs and vaccines which falls to AIFA and takes advantage of the collaboration of Regions and Autonomous Provinces, Local Health Authorities, Hospitals and Research Institutes (https://www.aifa.gov.it/web/guest/rete-nazionale-di-farmacovigilanza). All work together to ensure an adequate flow of information. Reports of suspected adverse reactions can be performed by doctors, by other health professionals and by citizens themselves. The Local Pharmacovigilance Contact Points, the Regional Pharmacovigilance Centres and AIFA check the reports on a daily basis, request any additional information and evaluate the causal link, each according to their own competences. The reports then flow from the national network to EudraVigilance, a European database managed by the EMA, and to the Uppsala Monitoring Center of the World Health Organization https://www.aifa.gov.it/sistema-europeo-eudravigilance.
The national pharmacovigilance system is also responsible for fostering more in-depth studies on pharmacovigilance and pharmacoepidemiology (the so-called active pharmacovigilance), as well as activities and initiatives to promote reporting and communication aimed at both citizens and healthcare professionals.

6. **How are reports taken into account?**
   Periodically, AIFA and the Regional Pharmacovigilance Centres perform in-depth assessments on the suspected adverse events reported (drugs and vaccines) to pinpoint any safety concerns. When several reports converge to describe the same type of phenomenon, a "signal" is identified. A signal is defined as a possible causal relationship unknown until then, or poorly documented previously, between an adverse event and a drug or vaccine. Normally multiple reports are required to generate a signal, depending on the severity of the event and the quality of the information available. The identification of the signal is followed by an in-depth study at a European level. In fact, any safety issue shall be assessed collectively at a European level with the involvement of EMA's Pharmacovigilance Risk Assessment Committee (PRAC). PRAC's assessments conclude with recommendations concerning the management as of that moment of the safety aspects relating to the phenomenon under investigation (see question number 10), which are regularly published on the EMA and AIFA website (https://www.aifa.gov.it/segnali-di-farmacovigilanza).

7. **In the case of these new vaccines, has the surveillance network been strengthened?**
   In view of the authorization of COVID-19 vaccines, several actions have been prepared to facilitate the collection, insertion and management of reports in the National Pharmacovigilance Network. In particular, specific instructions were provided to Local Contact Points and Regional Pharmacovigilance Centres, in accordance with the EMA provisions at a European level. Moreover, some active pharmacovigilance studies are being launched on people who have undergone vaccination which will allow us to collect as much information as possible on the safe use of vaccines in the real context.

8. **Who can I report a reaction to after vaccination?**
   Should you wish to report any event that occurred following the administration of the vaccine, you can contact your general practitioner/family doctor, the Vaccination Centre, your pharmacist or your Local Health Authority (ASL). The report can also be made directly by anyone who observes or becomes aware of it (both healthcare professionals and citizens), by filling in the form available on the AIFA portal (https://www.aifa.gov.it/content/segnalazioni-reazioni-avverse). The completed form shall be sent to the Local Pharmacovigilance contact point (RLFV) by e-mail or fax. Furthermore, it is possible to report directly online through the VigiFarmaco application by following the guided procedure (https://www.vigifarmaco.it/).

9. **What information shall be provided when submitting a report?**
   It is required to enter at least the following information:

   - initials of the name, age and sex of the person who experienced the suspected adverse event;
   - description of the type of event, as detailed as possible;
   - trade name and batch of the vaccine administered;
   - qualification and contact of the person submitting the report.

To facilitate the evaluation of adverse events following vaccination, it is also important to obtain information on the site of administration, time of vaccination, start time of the suspected adverse event, trend of symptoms and their evolution over time. AIFA or the Regional Pharmacovigilance Centre may request further information from those who submitted the report through the Local Pharmacovigilance Contact Point.
If the citizen himself/herself submits the report, it is important that s/he specifies everything s/he remembers, trying to be as precise as possible.

10. What happens if many reports indicate that a vaccine causes serious or unknown adverse reactions?

The evaluations, carried out continuously at national and community level (see question 6), will lead to different indications according to the different conclusions:

- the benefit/risk ratio of the product remains unchanged and it is not necessary to change the product information;
- the benefit/risk ratio of the product remains unchanged, but it is necessary to change the product information (summary of product characteristics and package leaflet);
- the risks outweigh the benefits of vaccination and the authorization of the vaccine can be suspended or revoked and the product withdrawn.

11. What are the most frequent adverse events or reactions? And what are their consequences for health?

The most frequently observed adverse reactions during the current vaccination campaign are local reactions at the injection site (e.g. pain, swelling, redness), fever, fatigue, headache and muscle or joint pain. These are non-serious reactions, of mild or moderate severity which, although annoying, resolve within a few hours or a few days, often without even resorting to symptomatic treatment (painkiller or similar).
As with all medicines, allergic reactions up to anaphylactic shock are also possible, although very rare. For this reason, vaccinations are carried out in a safe environment by trained personnel, and there is an observation period of at least 15 minutes after vaccination. Another aspect that is taken into account is that, following the injection, anxious reactions may also occur, with vaso-vagal phenomena ranging from the sensation of being about to faint up to actual fainting, so the staff pay attention to avoid fall injuries.
Monitoring of adverse reactions is described in the monthly surveillance reports available here.

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