EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Safety aspects of COVID-19 vaccines

European Commission webinar for healthcare professionals

Presented on 10 February 2021 by
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An agency of the European Union

Outline

- The European Medicines Agency's role
- Why conditional approval is the most appropriate tool in the EU?
- Which COVID-19 vaccines are authorised in the EU?
- How were the COVID-19 vaccines studied?
- What benefits and risks have been shown in studies?
- How long does protection from the vaccines last and can they reduce transmission?
- What about special populations?
- What information is still awaited for the COVID-19 vaccines?
- How is safety of vaccines studied from the development stage to use in real life?
- Safety monitoring of vaccines – why we need it and who monitors?
- How can you report side effects?

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What we do

Protect human and animal health

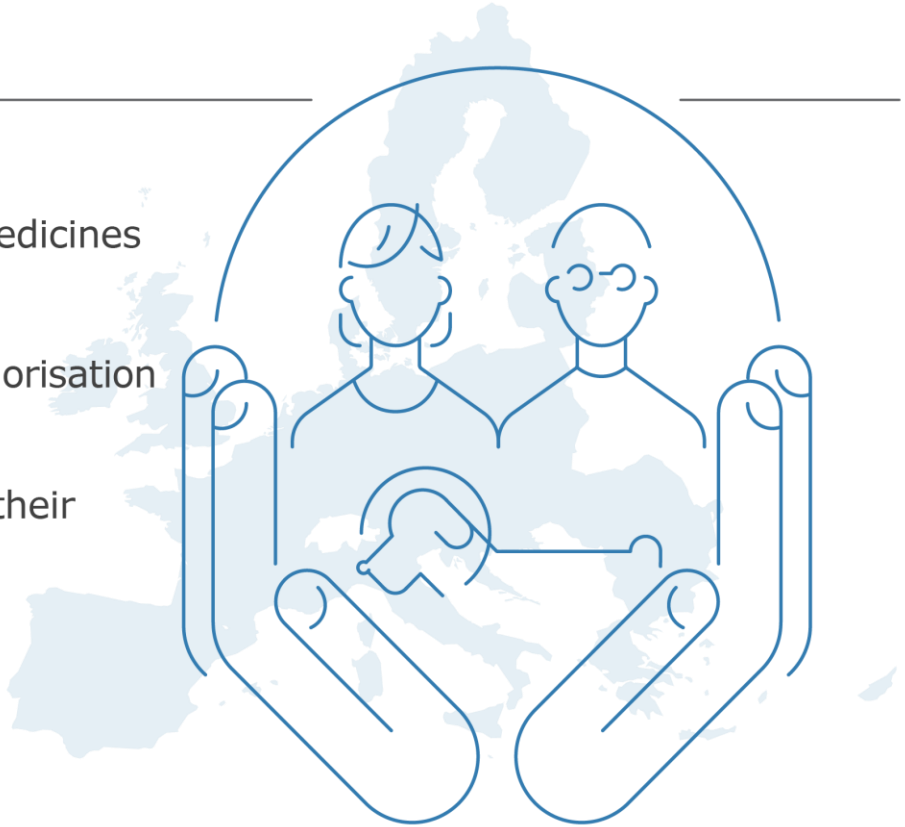
Facilitate development and access to medicines

Evaluate applications for marketing authorisation

Monitor the safety of medicines across their life cycle

ABC
XΨΩ

Provide reliable information on human and veterinary medicines to patients and healthcare professionals



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Who we are

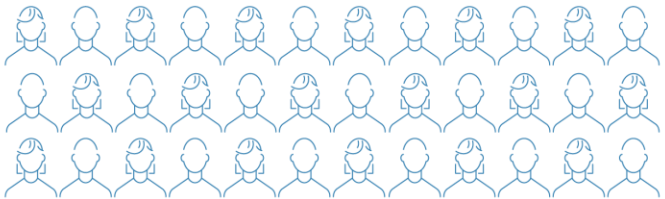
~4000 scientific experts from across Europe

7 Scientific Committees

- CHMP
- CVMP
- COMP
- HMPC
- PDCO
- CAT
- PRAC

1 Management Board

- 27 Member States' representatives
- 4 Civil society representatives
- 2 European Commission representatives
- 2 European Parliament representatives



1995 EMA established

~800 staff members

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Safety is paramount

- Vaccines only approved after demonstration that their overall **benefits outweigh their risks**
- Safety is paramount
- Because vaccine is given to healthy people, less risks can be accepted
- **COVID-19 vaccines** require **same types of studies** as for other vaccines
- **High** regulatory **standards** for Quality, Safety and Efficacy

Vaccines benefits in protecting people

Side effects or potential risks

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Conditional Marketing Authorisation

WHY CONDITIONAL APPROVAL IS THE MOST APPROPRIATE TOOL IN THE EU?

- **Formal approval** of a medicine across the EU: **all member states benefit** from the joint scientific assessment and approval
- It has **all safeguards and controls** in place to ensure high level of protection to citizens during a mass vaccination campaign:
  - A robust **monitoring plan** for managing **safety**
  - Clear **legal framework** for evaluation of **emerging efficacy data**
  - **Manufacturing** controls including **batch controls** for vaccines
  - Full **prescribing information** and **package leaflet** with defined conditions for storage and use of the vaccine
  - A **plan** for **use** of the vaccine **in children**
  - **Additional studies or other data** ('conditions') that the company is **legally obliged** to provide with defined **timelines**

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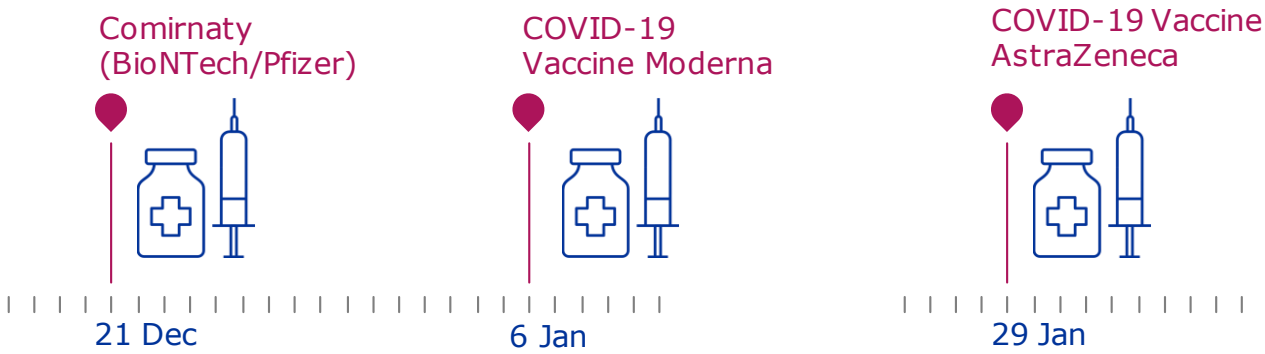
Which COVID-19 vaccines are authorised in the EU?



- Currently three COVID-19 vaccines are **authorised in the EU**
- Two contain **messenger RNA (mRNA)** with instructions for producing a protein from SARS-CoV-2, the virus that causes COVID-19 (Comirnaty and Moderna)
- The AstraZeneca vaccine is a **viral vector vaccine** made up of another virus that has been modified to contain the gene for making a protein from SARS-CoV-2
- The vaccines do not contain the virus itself and cannot cause COVID-19

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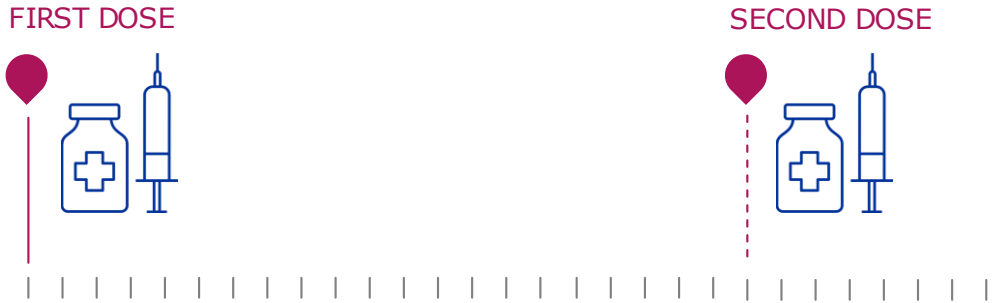
How are the COVID-19 vaccines used?



- These vaccines are all given as **two injections**, usually into the muscle of the upper arm
  - Comirnaty (BioNTech/Pfizer) is given **3 weeks apart**
  - COVID-19 vaccine Moderna (Moderna Biotech Spain, S.L.) is given **28 days apart**
  - COVID-19 Vaccine AstraZeneca is given between **4-12 weeks apart**
- You can check the specific conditions of use for the vaccines, **in the package leaflet or in the prescribing information**

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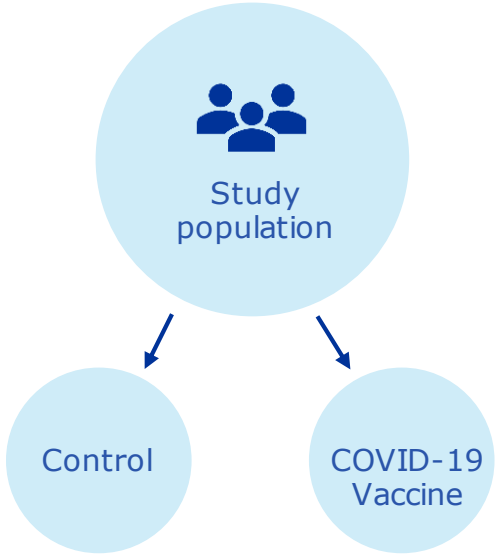
How were the COVID-19 vaccines studied?

- The main trials involved **very large numbers of people**:
  - around **44,000** for Comirnaty
  - around **30,000** for Moderna vaccine
  - around **24,000** for AstraZeneca vaccine
- Half received the vaccine and half were given a control
- People did not know whether they received the vaccine or the control



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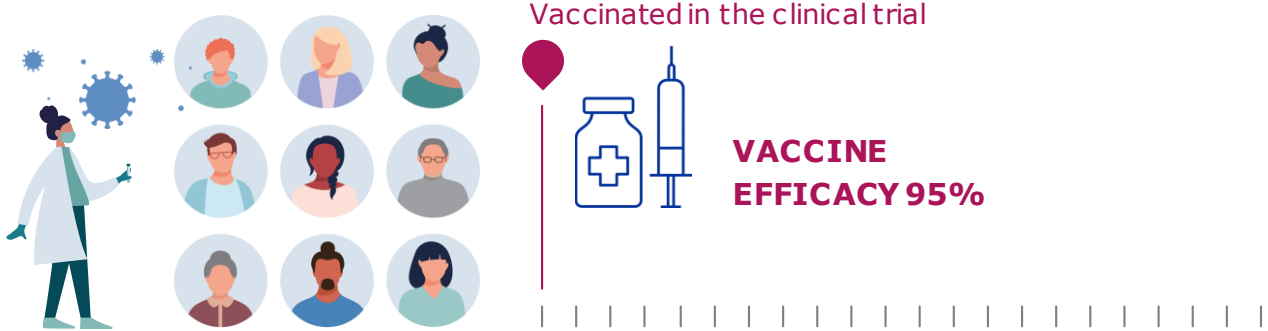
Comirnaty – main benefit identified in study



How many people developed COVID-19 with symptoms?

18,325 people given placebo → **162**

18,198 people given Comirnaty → **8**

Full information on the benefit-risk assessment for Comirnaty

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Comirnaty – main side effects identified in main study

MAIN SIDE EFFECTS

- Most common side effects **(more than 1 in 10 people)** usually mild or moderate and temporary, including pain and swelling at injection site, tiredness, 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, pain in the limb, enlarged lymph nodes, difficulty sleeping and feeling unwell were uncommon side effects **(less than 1 in 100 people)**
- Weakness in muscles on one side of face (acute peripheral facial paralysis or palsy) occurred rarely in **less than 1 in 1,000 people**
- **Very small number of cases of severe allergic reactions** (anaphylaxis) seen in vaccination campaigns

Full list of side effects for Comirnaty

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COVID-19 Vaccine Moderna – main benefit identified in study

Vaccinated in the clinical trial

VACCINE EFFICACY 94,1%

How many people developed COVID-19 with symptoms?

14,073 people given placebo → **185**

14,134 people given Moderna → **11**

Full information on the benefit-risk assessment for COVID-19 vaccine Moderna

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COVID-19 Vaccine Moderna – main side effects identified in study

MAIN SIDE EFFECTS

- Most common side effects **(more than 1 in 10 people)** usually mild or moderate and temporary, including pain and swelling at injection site, tiredness, chills, fever, swollen or tender lymph nodes under the arm, headache, muscle and joint pain, nausea and vomiting.
- Redness, hives and rash at the injection site and rash occurred in **less than 1 in 10 people**.
- Itching at the injection site occurred in **less than 1 in 100 people**.
- Swelling of the face, which may affect people who had facial cosmetic injections in the past, and weakness in muscles on one side of face (acute peripheral facial paralysis or palsy) occurred rarely **(less than 1 in 1000)**.
- **Very small number of cases of severe allergic reactions** (anaphylaxis) seen in vaccination campaigns.

Full list of side effects for COVID-19 vaccine Moderna

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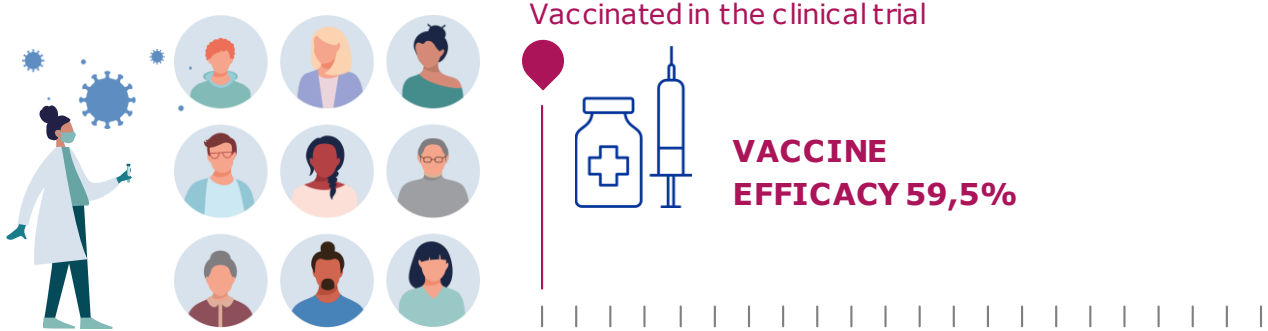
COVID-19 Vaccine AstraZeneca – main benefit identified in study



How many people developed COVID-19 with symptoms?

5,210 people given control	→	**154**
5,258 people given AstraZeneca	→	**64**

Full information on the benefit-risk assessment for COVID-19 vaccine AstraZeneca

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COVID-19 Vaccine AstraZeneca – main side effects identified in study

MAIN SIDE EFFECTS

- Most common side effects **(more than 1 in 10 people)** usually mild or moderate and temporary, including pain and tenderness at injection site, headache, tiredness, muscle pain, general feeling of being unwell, chills, fever, joint pain and nausea.
- Vomiting and diarrhoea occurred in **less than 1 in 10 people**.
- Decreased appetite, dizziness, sweating, abdominal pain and rash occurred in **less than 1 in 100 people**.
- Allergic reactions have occurred in people receiving the vaccine.

Full list of side effects for COVID-19 vaccine AstraZeneca

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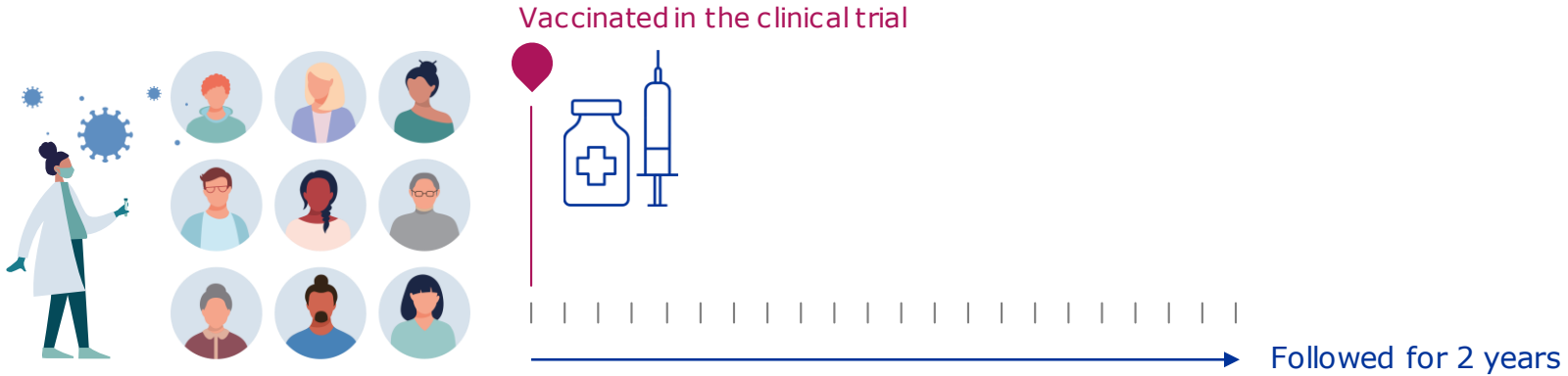
How long does protection from the vaccines last?



- It is not currently known **how long protection given by the vaccines lasts**
- The people vaccinated in the clinical trial will **continue to be followed for 2 years** to gather more information on the duration of protection

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Can the vaccines reduce transmission of the virus from one person to another?

- It is too soon to know the wider **impact of vaccination** on the spread of the SARS-CoV-2 virus in the community
- It is not yet known to which extent vaccinated people may still be able to carry and spread the virus – trials ongoing
- **The precautions must not be relaxed even after vaccination**: people should continue to **keep distance** from other people, **wear face masks and wash hands**
- It is important to **continue following national and regional guidelines**, which will be determined by the level of transmission locally

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Can people who have already had COVID-19 be vaccinated?

- **Not enough data from the trials** to conclude on the added-benefit of how well the vaccines work for people who previously had COVID-19
- **Trials included a few people** who were seropositive for SARS-CoV-2 but did not report history of COVID-19 (which was excluded from the study)
- There were no additional side effects in these people

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Can children / immunocompromised patients be vaccinated?

- The vaccines are currently **not approved for younger children:**
  - **Comirnaty** can be given above **16 years of age**
  - **Moderna** can be given above **18 years of age**
  - **AstraZeneca** can be given above **18 years of age**

- There are limited data on **immunocompromised people** (people with weakened immune systems):
  - Although immunocompromised people may not respond as well to the vaccine, there are no particular safety concerns. Immunocompromised people can still be vaccinated as they may be at higher risk from COVID-19

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Can pregnant or breast-feeding women be vaccinated?

- Data on the use of the authorised COVID-19 vaccines during pregnancy are **very limited**
- Non-clinical studies (e.g. animal studies) do not show any harmful effects in pregnancy
- Although there are no studies on breast-feeding, **no risk for breast-feeding is expected**
- The decision on whether to use the vaccine in pregnant women should be made in close consultation with a healthcare professional after considering the benefits and risks

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Can older people be vaccinated?

- **Comirnaty:** study included people over 75 years of age. Efficacy was calculated in over 36,000 people from 16 years of age (including people over 75 years of age). No differences in frequency of side effects were observed in people aged over 70 years compared to the age group over 55 years. No specific safety concern is anticipated for the elderly.

- **Moderna:** study included people aged 65 years or older. Efficacy was calculated in around 28,000 people from 18 to 94 years of age. The observed safety profile in older adults does not give rise to concerns.

- **AstraZeneca:** most study participants were between 18 and 55 years. Too few results exist for participants over 55 years to provide a figure for how well the vaccine will work in this group. Protection is expected, given that an immune response is seen in this age group. As there is reliable information on safety in this population, it is considered that the vaccine can be used in older adults. More information is expected from ongoing studies, which include a higher proportion of elderly participants.

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How well do COVID-19 vaccines work for people of different ethnicities and genders?

- **The main trials** included people of different ethnicities and genders
- **High efficacy** levels were maintained across genders, racial and ethnic groups

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VACCINES APPROVED IN THE EU

What information is still awaited for the COVID-19 vaccines?

- The companies that market COVID-19 vaccines will continue to provide results from the **main studies, which are ongoing for 2 years**
- These trials and additional studies will provide information on how long protection lasts, how well the vaccine prevents severe COVID-19, how well it protects immunocompromised people, children and pregnant women, and whether it prevents asymptomatic cases
- In addition, independent studies of COVID-19 vaccines coordinated by EU authorities will also give more information on the **vaccine's long-term safety and benefit in the general population**
- The companies will also carry out studies to provide additional assurance on the pharmaceutical quality of the vaccine

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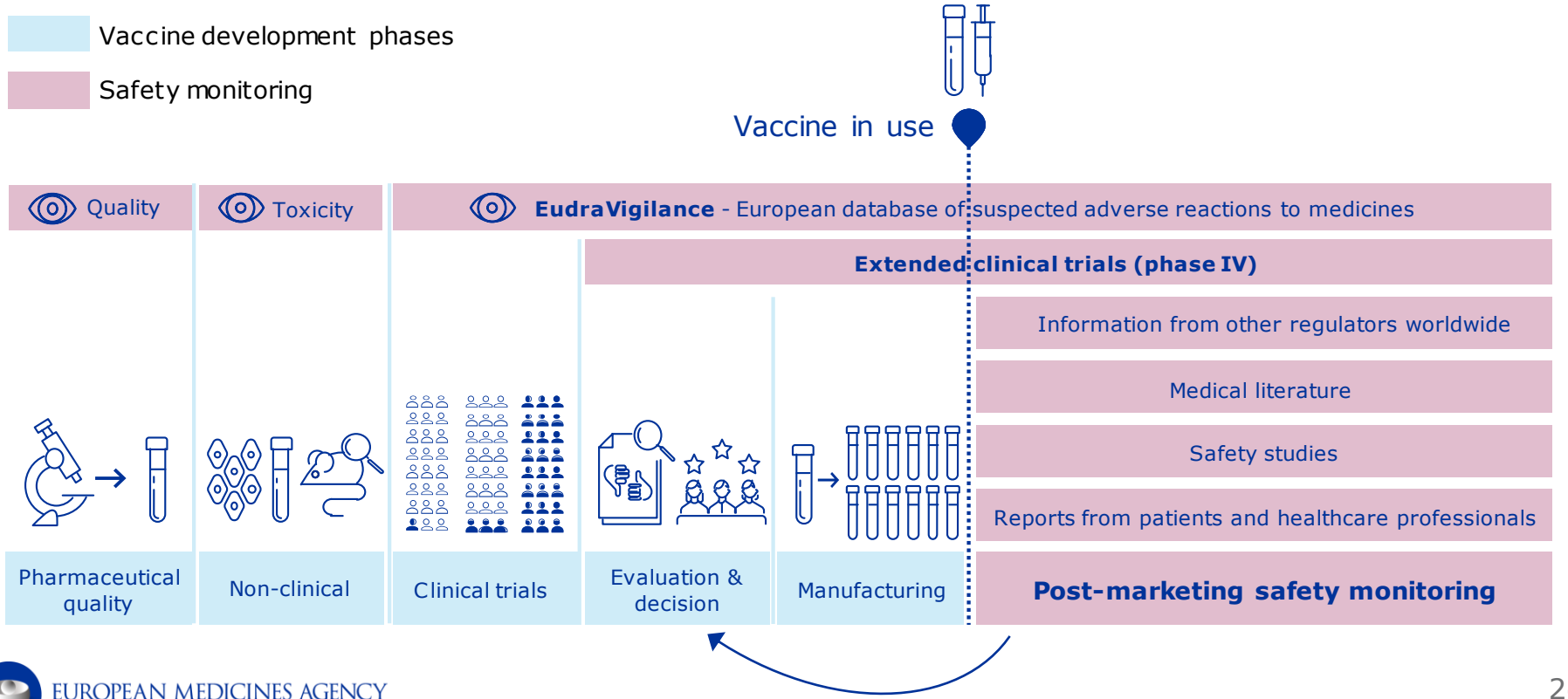
How is safety of vaccines studied from the development stage to use in real life?



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Why do we need to monitor the safety of medicines after approval?

- All medicines, including vaccines, have **benefits and risks**
- **At the time of approval:** evidence comes mainly from controlled, randomised clinical trials
- **After approval:** medicines will be used in real conditions by a far larger population
- Post-marketing **safety monitoring** is important **to identify** any new or changing risk as quickly as possible, and **take action**
- COVID-19 vaccines to be used in millions of EU citizens in a short time;
  - Due to large number of vaccinated people we need to ensure safety monitoring **reacts quickly**
- **Additional resources** are being mobilised to closely monitor safety and assess new information

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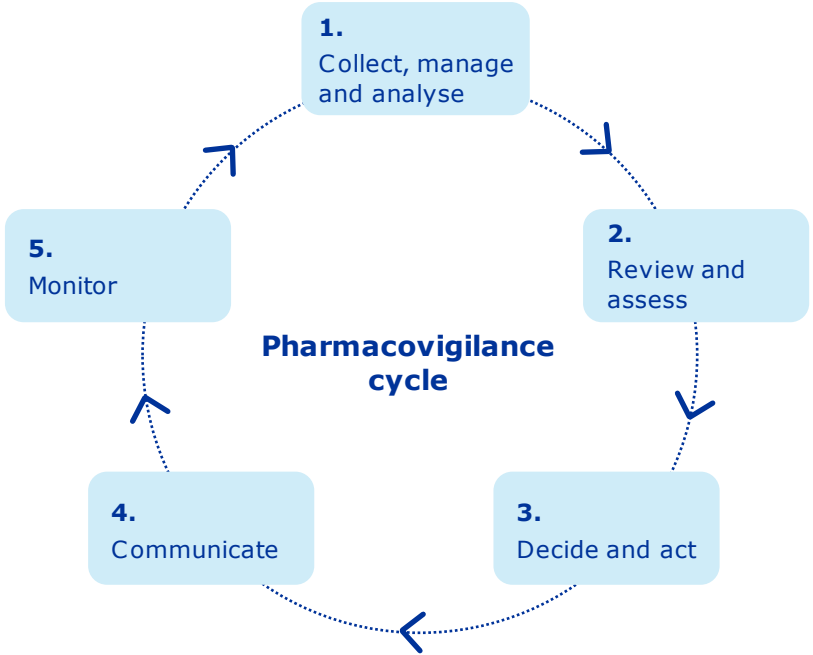
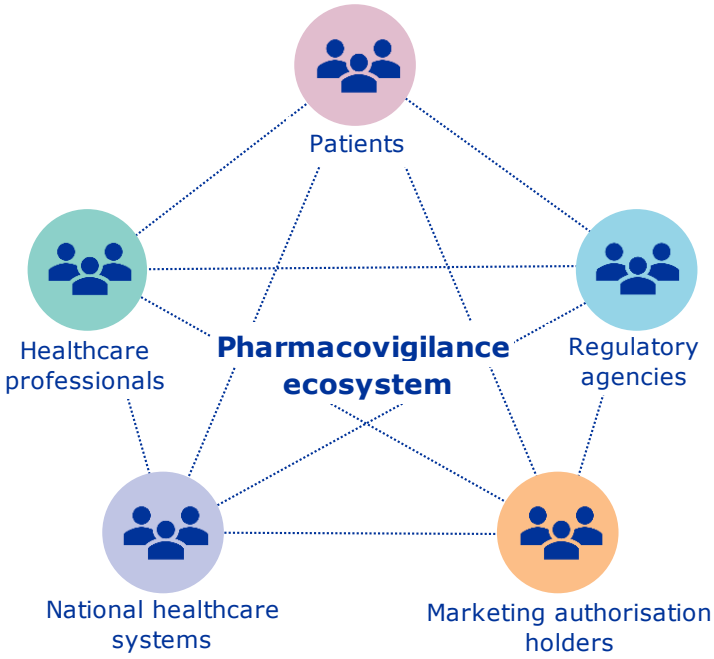
Who does the safety monitoring in the EU?

The EU has a comprehensive **safety monitoring** and **risk management** system known as the **EU pharmacovigilance system**





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How will the safety of vaccines continue to be monitored after approval?

Safety monitoring after approval is needed to detect any new or changing side effects. This includes:

- **Intensive analysis** of reports of suspected side effects from patients and healthcare professionals (also referred to as spontaneous reporting collected in EudraVigilance, the European database of suspected side effects)
- **Post-authorisation safety studies** conducted by the vaccines' manufacturers, as required by regulators
- **Additional studies** performed in Europe on the safety of vaccines when used in real life (also referred to as observational studies)
- **International collaboration** on COVID-19 vaccine monitoring

Risk management plan (RMP)

- Specifically developed for each approved vaccine, following EU guidelines
- Contains important information about the vaccine's safety, how to collect further information and how to minimise any risks
- Continually updated as more information becomes available

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What studies will be undertaken by regulators in the context of the COVID-19 pandemic?

2020
ACCESS PROJECT

Set up a European infrastructure for vaccine monitoring

- Gather background information on key adverse events
- Establish an EU network of data sources
- Develop template protocols for vaccine coverage, effectiveness, and safety studies

2020/2021
EARLY MONITORING STUDY

Additional early safety monitoring to complement spontaneous reporting systems

- Primary data collection using an app-based application to gather incidence rates of adverse events
- Complemented by secondary analysis of healthcare data for rapid signal assessment
- In priority groups, for one year, in at least 5 EU Member States

2021/2022
LARGE MONITORING STUDIES

Additional EMA-funded safety studies

- Active surveillance, building on the early monitoring study
- Additional studies for rapid evaluation of any potential safety signals

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How can you report side effects?

- **Reporting** suspected **side effects** following vaccination is critical
- **Anyone can report** a suspected side effect to their national authority or the vaccine manufacturer
- All reports are sent to **EudraVigilance, the European database** of suspected side effects where
  - the data are analysed to detect new side effects
  - and anonymised data are made public for all to review
- **Please report** suspected side effects
  - As vaccines are biologicals released in batches, the batch number is important for reporting purposes

http://www.adrreports.eu/

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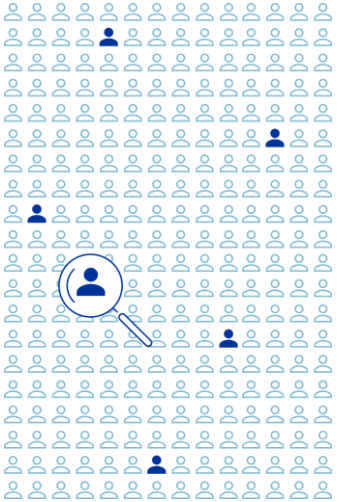
How does EMA assess if side effects are caused by the vaccine?

- **Established analysis techniques** are in place to assess whether a side effect is likely to be caused by the vaccine
- Since millions of people will be getting the vaccine in a short time, many of them will develop illnesses for other reasons in close proximity to vaccination
- If these occur just after vaccination, they may be reported as suspected adverse reactions to the vaccine, when the **association** was just **due to chance**
- If analysis concludes that a **new** side effect is caused by a vaccine, it is included in the package leaflet
    - For example, a very small number of severe allergic reactions (anaphylaxis) have occurred in vaccination campaigns outside the EU an this new information was assessed and reflected in the package leaflet



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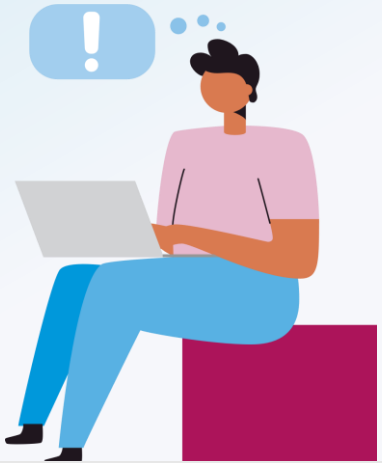
Conclusions

- **COVID-19 spreads quickly** and causes severe disease, death and large burden to healthcare systems
- **Three COVID-19 vaccines are now approved in the EU** – robust and efficient scientific assessment
- The vaccines have been shown to offer an adequate level of protection against COVID-19 disease
- It is still **too soon** to know the **wider impact** on preventing infection, asymptomatic transmission and viral spread in the community – until then measures like masks and physical distancing are important
- **Vaccination is important** to prevent people getting sick with COVID-19 disease
- Fewer people expected to go to hospital, **reducing the burden on healthcare** and freeing up resources to treat other illnesses



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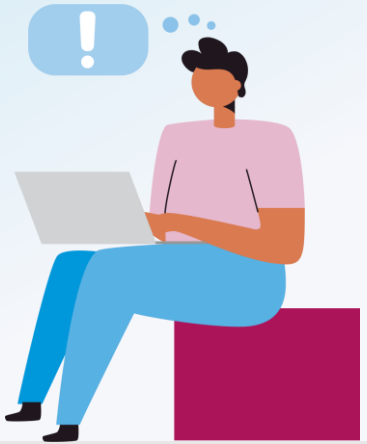
Conclusions

- No medicine is 100% safe so like any other medicines, vaccines can have side effects
- The majority are mild, and even rare, serious side effects must be balanced against the prevention of severe or even fatal disease like COVID-19
- A strong EU pharmacovigilance system is in place; **safety will not be compromised**
- **Unprecedented** steps are being taken to monitor safety in practice, to be transparent and to take action immediately
- COVID-19 vaccine safety will be **stronger with your participation**
- **Please report suspected side effects**



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Any questions?

Further information

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Where can I find more information for each COVID-19 vaccine?

- Comirnaty
- COVID-19 Vaccine Moderna
- COVID-19 Vaccine AstraZeneca

- Medicine overview addressing questions and answers in lay language; available in all EU languages
- Risk management plan (RMP)

- Recommendations and precautions to be followed by
  - healthcare professionals (summary of product characteristics) and
  - patients (package leaflet)

  for the safe and effective use of each approved vaccine; available in all EU languages

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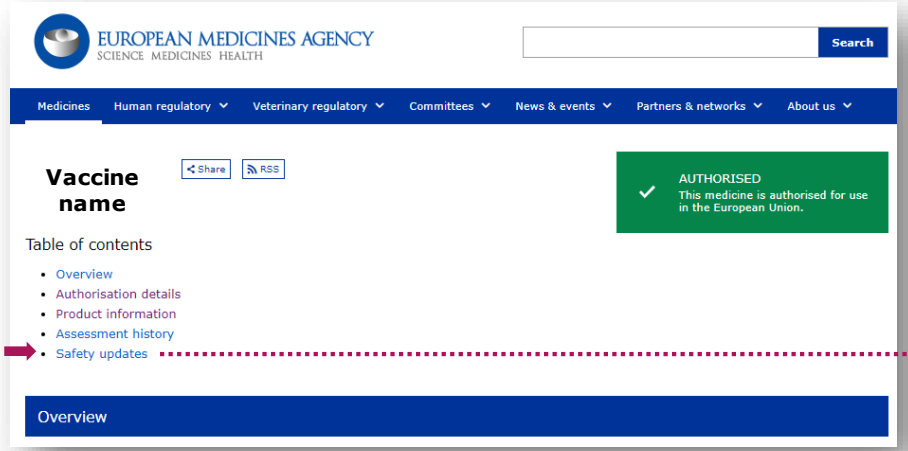

- Provide the outcomes of the assessment of emerging data since marketing authorisation for COVID-19 vaccines.
- The assessments are carried out by EMA's safety committee (Pharmacovigilance Risk Assessment Committee (PRAC)).
- The safety updates are published regularly.

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