COVID-19 Vaccine Questions and Answers for Healthcare Providers

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The CONSIDER Working Group

In recognition of the critical importance of COVID-19 vaccines and the need to understand their safety, the **CONSIDER** (**CO**vid-19 vacci**N**e **S**afety quest**I**ons an**D** h**E**althcare p**R**oviders) Working Group (WG) was created in September 2020.

The **CONSIDER WG** aims to provide clear, comprehensive answers to questions pertaining to COVID-19 vaccine safety prior to, and during the vaccines roll out to
1) facilitate scientific discussion between stakeholders, including front line health workers with potential vaccine recipients and
2) increase comprehension and transparency of information to facilitate acceptance and uptake.

There are likely to be concerns associated with COVID-19 vaccines given the accelerated pace of vaccine development, mistrust of the pandemic response by governments and growing suspicion regarding vaccines in some population groups.[1-4] As for all new vaccines, there is the possibility that rare adverse reactions will not be identified in clinical trials and only found once a large number of people are vaccinated. Additionally, when vaccinating large number of people, some of them will have adverse health outcomes shortly after vaccination by chance alone. COVID-19 vaccine safety concerns need to be urgently addressed. The **CONSIDER** group was developed to provide responses to common COVID-19 vaccine safety questions that are understandable and accessible to key stakeholders.

Science is evolving rapidly. As more questions come to the group's attention or more information becomes available (from COVID-19 vaccine clinical trials and early experience with vaccine introduction in countries), the answers will be updated and new answers will be posted. The questions and answers are hosted on this page and are cross-referenced on other sites.

The information provided on this page is written by an international group of experts in immunization and is applicable globally, including in the Canadian context.

Below is the latest version of the answers. This webpage will be updated as new answers are added.

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Can mRNA vaccines “genetically modify" humans and are there other safety concerns with these vaccines?

Sonali Kochhar and the Q&A Team

Messenger RNA (mRNA) vaccines consist of synthetic pieces of message RNA encapsulated by a lipid nanoparticle (LNP) for delivery into a host cell. The mRNA vaccines are not live virus vaccines, the lipid nanoparticle has a stabilization and/or adjuvant effect and the vaccines do not use an additional adjuvant to enhance vaccine efficacy.[1] The mRNA vaccines do not enter the nucleus and they cannot be integrated into the human DNA or cause changes to the human DNA in vaccine recipients.[1,2,3,4]

Following an injection into the upper arm muscle, the COVID-19 mRNA vaccines will give instructions to the cells to make a harmless piece of protein called “spike protein.” The spike protein is found on the surface of the virus that causes COVID-19. After the protein pieces are made, the cells break down the mRNA (the instructions to make the protein) i.e. there is natural degradation of the vaccine within days.[1,2,3]

The protein pieces are displaced onto the surface of the cell. The immune system recognizes that the protein does not belong to the cell and starts making antibodies, and building an immune response (i.e. there is induction of both B and T cells response), exactly like what happens following natural infection against COVID-19. The body learns to protect itself against future COVID-19 infection without the risk of the serious consequences of a COVID-19 infection.

mRNA is an intrinsically safe vector for a vaccine as it is transient and a minimal carrier of information that does not interact with the vaccine recipient’s DNA. The lack of genomic integration along with mRNA being non-replicative and decaying metabolically within a few days makes mRNA a safe and transient carrier of information.[2,3]

trigger the immune system to target specific cancer cells. In the future, mRNA technology may allow one vaccine to provide protection against multiple diseases, thus decreasing the number of injections required for protection against these multiple diseases.[1] The fast and highly scalable mRNA manufacturing and LNP formulation processes enable rapid production of many vaccine doses.[2,3] This makes mRNA vaccines suitable for rapid vaccine development in a pandemic.[5] mRNA vaccines offer maximum flexibility in the development process as any protein can be expressed by the human body from mRNA without the need to adjust the production process.[3]

Given the composition of mRNA vaccines, there is a need for very careful storage and handling to ensure the stability of the mRNA. For example the Pfizer mRNA COVID-19 vaccine (BNT162b2) needs to be stored between -80°C to -60°C (-112°F to -76°F) and after thawing and dilution prior to administration, it must be stored between 2°C to 25°C (35°F to 77°F) and used within 6 hours from the time of dilution. The Moderna mRNA COVID-19 vaccine (mRNA-1273) can be stored at -20°C (-4°F), equal to most medical freezer temperatures, for up to 6 months and after thawing, at 2° to 8°C (36° to 46°F) for up to 30 days within the 6-month shelf life. The technology over time may work to overcome this issue but at the present time this does limit access and use in many settings where ultracold freezer and even minus 200C access is an issue. mRNA vaccines are a huge advancement in vaccinology that will over time change the field.

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How is vaccine safety determined prior to vaccine use?

Eve Dubé and Q&A Team

Unlike drugs that are given to ill people for cure, vaccines are given to healthy people to prevent disease. Thus, vaccines usually require higher proof of safety than therapeutic drugs before being used. Vaccine development undergoes a rigorous set of carefully implemented scientific and ethical processes and procedures to ensure safety and efficacy of vaccines before they are given to a large number of people (see MacDonald and Law[1] on the Canadian vaccine safety system, very similar approaches are used in many other countries).

First, vaccine safety and immunogenicity (i.e., ability of the vaccine to produce an immune response) are assessed in pre-clinical studies using tissue-culture, cell-culture or animal models (e.g., tests with mice, ferrets or monkeys). If pre-clinical studies are successful (both safety and immunogenicity), clinical studies with humans are conducted. At each stage, the data of the studies and trials are assessed by government regulators to give permission to move to the next stage.

Phase I trials involve a small group of adults (generally between 20-100 healthy volunteers) and aim to assess the safety of the vaccine and the type and extent of immune response. If no issues are identified during Phase I, the experimental vaccine progresses to Phase II trials involving several hundreds of individuals. The goal of Phase II trials is to assess the vaccine's safety, immunogenicity, dosing, and schedule. If successful, larger Phase III trials are conducted with thousands to tens of thousands of people to assess efficacy and further study safety. These are randomized and double-blind trials where the candidate vaccine is being tested against a comparison or placebo (usually an inert substance, such as a saline injection). Phase III Trials allow for the detection of rare side effects that are too infrequent to be identified in Phase I or Phase II Trials (e.g., occur in less than 1 to 10/10,000).[2]

The information on vaccine safety and efficacy from these trials is then assessed by government regulators who are independent from the researchers who conducted

vaccine can be used in that country. Vaccine safety still continues to be monitored once the vaccine has been approved through active and passive surveillance to ensure that possible risks of very rare side effects associated with the vaccine are identified (reference to last question in the section on long term effect).

COVID-19 vaccine development is following these standards, even if the vaccines are being developed rapidly (reference to Question 4).[3] Many COVID-19 vaccines are developed using approaches and technologies that have proven safe with other vaccines or drugs in the past, others use novel technologies. As with all new vaccines, great care and attention will be paid to vaccine safety.

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What measures ensure safe vaccines?

Janice Graham and Q&A Team

Many checks (laws, regulations, and guidelines) help ensure the vaccines approved by National Regulatory Authorities (NRAs), such as the U.S. Food and Drug Administration, Health Canada, and the European Medicines Agency (EMA), are safe and efficacious. NRAs oversee the approval of clinical trials and carefully evaluate the evidence before a vaccine or therapeutic drug or device is approved in

decision-making capacity, trial conduct, fairness and equity in research participation, privacy and confidentiality, conflicts of interest, safety monitoring and reporting, and registration (e.g., Canada's Tri-Council Panel on Research Ethics). International bodies, e.g., the International Conference on Harmonization (ICH) of Good Clinical Practice guideline, oversee research in humans and regulatory obligations for safety, efficacy and quality.[1]

Each clinical trial has a Data Safety Monitoring Board that evaluates interim data at predetermined intervals during the trial. Trials are paused when an untoward event occurs and can be stopped completely if continuation is deemed to be unmerited. The World Health Organization (WHO) coordinates expert advisory panels to deliberate on matters of global health, provides ethical guidance, and works with NRAs to license safe vaccines in low income countries. WHO encourages countries to have an independent national immunization technical advisory group (NITAG) to review the approved vaccine data in respect of the local epidemiology to determine who, if any, should receive the vaccine. NITAGs build capacity for global vaccine safety standards.[2,3]

Transparency throughout the vaccine pre-approval lifecycle is critical for safety and public trust, including review of all trial protocols, all data and technical documents, clinical study reports, stopping rules, and decision-making processes.[4,5] Exceptional needs for urgent research during public health emergencies can guide ethics review and create mandates for NRAs to expedite regulatory pathways for clinical trials, consider conditional approvals and/or issue emergency use authorization. Despite some political pressure, NRAs in Canada, US and Europe have resisted taking shortcuts. Faster approval requires vigilance to ensure safety is not compromised.[6,7,8]

Regulatory and legal standards limiting conflict of interest, enforcing manufacturing quality and the reporting of serious AEFIs ensure safety. To instill confidence that expedited COVID-19 vaccines will be safe, the public needs assurance of:

1. Clear disclosure guidelines that exclude those with perceived conflict of interest (personal and professional) from being involved in decisions;

making processes and rationales;

3. No increased participant risk from modifications made in adaptive trials that compress testing phases or add new arms in response to new findings. If, as GAVI states "These changes aren't guesswork - they are based on clearly defined rules that have been set up by scientists who are experts at evaluating uncertainty",[9] these modifications should be made immediately known, i.e., transparent, with rationale and data/evidence supporting those decisions;
4. Independent appraisal of all clinical trial evidence and decision-making rationale, advisory committee recommendations and vaccine promotion to address perception of conflict of interest;
5. Sufficiently powered trials to ensure safety as well as efficacy. Phase III trials can miss rare (occurrence rate ≥ 0.01% and < 0.1%) but serious adverse events if trial participant numbers are small. Large trial populations are important in identifying rare and very rare but serious AEs that can result in morbidity (e.g., intussusception with Rotashield);
6. Post-approval monitoring and active surveillance must be in place to detect very rare but serious adverse events following vaccination as well as detection of vaccine failures;
7. Disease prevention rather than surrogate (e.g. serological) endpoints are a higher standard;
8. Locating Phase III trials where the disease is prevalent is critical to disease exposure and the determination of disease prevention;
9. With no available cures for COVID-19, human challenge trials are currently unethical.
10. Equitable participation in research of under-represented communities at risk for serious disease, i.e., older adults, racial/ethnic groups, pregnant and immunocompromised persons.

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Why was the Oxford vaccine clinical trial stopped and how was the vaccine safety determined?

Hanna Nohynek and Q&A Team

One study participant developed weakness in the arms and legs after vaccination,

that another participant had been diagnosed with multiple sclerosis, which also was deemed to be unrelated to the COVID-19 vaccine.[1] In large trials with tens of thousands of participants, these types of pauses are not uncommon. Illnesses can happen by chance but must be independently reviewed to clarify whether or not they are linked to the medicine or vaccine being studied. In this case, the independent experts came to a conclusion that the vaccine did not cause these events, and the study was allowed to continue recruiting in the UK, South Africa, Brazil, Japan and the US.

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Vaccine Introduction in Countries

What are the critical roles of front line health care workers in contributing to the knowledge about the effectiveness and safety of approved COVID-19 Vaccines?

Noni E MacDonald and the Q&A Team

While post approval Phase IV trials (post-marketing surveillance trials) of COVID-19 vaccines are required in many countries by their National Regulatory Authority who approved the vaccines, these trials are often not large enough to detect vaccine failures, nor very rare serious adverse events attributable to the vaccines.

Key contributions of front line health care professionals (HCP) in determining vaccine effectiveness and safety include

A) Detection of vaccine failure cases

the "real world" performance of these vaccines i.e. effectiveness. A vaccine's effectiveness may be influenced by many factors including age, presence of underlying health conditions, context, gender, medications, nutrition status and strictness of immunization program adherence to storage and delivery requirements to name a few. Hence, once each COVID-19 vaccine is approved, we need to know how well it works in the "real world" across the broad range of people who need to be immunized to protect themselves and their communities. In any country once COVID vaccines are in use, front line HCPs need to check all patients who present with clinical findings suggestive of COVID-19 infection to determine if they have received a COVID-19 vaccine and if so which one, the number of doses and when each was taken. This might be done by checking the national immunization register if one exists, the patient's health records and also by asking the patient directly. If the patient has received a COVID-19 vaccine, the patient's COVID infection diagnosis must be verified not by clinical findings but by a gold standard test such as a real-time polymerase chain reaction (RT-PCR) test of respiratory tract materials during the first week of symptoms.[1,2] Rapid point of care tests may be used but RT-PCR is preferable to minimize the risk of a false positive test, a concern highlighted by the US Food and Drug Administration (https://www.fda.gov/medical-devices/letters-health-care-providers/potential-false-positive-results-antigen-tests-rapid-detection-sars-cov-2-letter-clinical-laboratory). For the COVID-19 vaccines using the spike protein as the antigen, routine serological testing is not helpful in confirming the COVID diagnosis because of the positive COVID immunization history. Nucleic capsid antibody assay is required. Along with providing care for the patient, the HCP needs to report suspected vaccine failure cases to public health for follow up investigation to determine if indeed a vaccine failure has occurred and if so why. The details are important for determination of effectiveness of the implicated vaccine:

- Is the failure directly due to the specific vaccine and/or was it a storage/handling, diluent or other program error? What was the specific setting?
- Are there underlying clinical reasons that may have altered the response of this patient to the specific vaccine?
- Are failures being seen amongst others who received that specific vaccine

- Is there evidence of waning protection over time? Does this vary by age, by subgroup or by other factors?

As vaccine failure cases accumulate, effectiveness differences might be seen with the different vaccines in different ages, subgroups and settings. This information is important locally, nationally and globally. Depending on the findings, modification to the recommendations for use of the specific vaccine may need adjustment for different age groups and/or subgroups- e.g. more doses, different intervals, need for booster doses etc. as well as being able to offer more specific advice about the interval between receipt of vaccine doses and protection.

B) Detection of very rare but serious Adverse Events Following Immunization (AEFI)

Assessing any new vaccine for safety is a complex process. [3] Individual and community vaccine acceptance concerns may arise when an AEFI is reported on in the public media, and there is insufficient information also offered by authorities and experts on the event and steps being taken to better understand causality.

An AEFI is “any untoward medical occurrence that follows immunization and that does not necessarily have a causal relationship with the usage of the vaccine” [4]. A serious AEFI is an event that is life-threatening or leads to death, hospitalization, significant disability or congenital anomaly. [4] However, just because an AEFI has occurred this does not mean it is causally related to the vaccine, its manufacturing, the immunization program process or the immunization procedure, it may have been coincidental i.e. unrelated event.

Pre-licensure clinical trials are able to detect common AEFIs (i.e. those that occur in 1% to 10% of recipients) such as a sore arm, poor appetite, local site redness, mild fever etc. As they are usually mild, self-limited problems, they do not preclude vaccine approval by the regulator if the occurrence rate is not excessive.
Reassuringly, the Phase I, II and III pre-licensure clinical trials data from one mRNA vaccine and one adeno virus vector vaccine moving to approval in several countries as of December 2020 have not reported serious vaccine safety concerns according

candidate in US trial.

The number of participants in these pre-licensure clinical trials even if relatively large like 30,000 or more are still not sufficient to detect very rare serious adverse events to occur i.e. those that occur in less than 0.01%. HCP must remember that for COVID vaccines, these serious but very rare AEFI would still be much less common than serious events due to COVID-19 disease itself i.e. COVID complications, hospitalization and even death due to COVID-19. [8,9,10] Serious but very rare AEFI can only be detected post approval as millions are immunized; however, there is a wide variation amongst countries in their capacity to carry out post approval vaccine safety surveillance for serious AEFI (https://www.who.int/vaccine_safety/publications/2019_Landscape_Analysis.pdf?ua=1).

Regardless of whether only a passive AEFI surveillance system is in place or if an active one is in place with routine searching for safety signals [11], front line HCPs play a key role in detecting these cases and alerting public health that a serious AEFI may have occurred. All front line HCPs not only need to know how to report a serious AEFI in their setting but also not to jump to the conclusion that the vaccine caused this serious AEFI. Such determination needs to be done by an independent Causality Assessment Committee in the country (https://www.who.int/vaccine_safety/publications/CausalityAssessmentAEFI_EN.pdf?ua=1). This committee determines, using a systematic case review process, if the reported event (specific diagnosis) was due to the vaccine, to a vaccine manufacturing error, an immunization program error, an immunization stress related response or was a coincidental unrelated event. The World Health Organization has developed a COVID-19 Vaccines: Safety Surveillance Manual to help countries carry out this important task. (https://www.who.int/vaccine_safety/committee/Module_Establishing_surveillance_systems.pdf?ua=1). Beyond reporting the serious AEFI, front line HCP often also have a relationship with the patient and the family and are well placed to communicate the steps being taken to ascertain the role the vaccine did or did not play in the serious AEFI. The importance of not jumping to conclusions prematurely needs to be emphasized. Public health and the immunization program need to work hand in hand with the front line HCP to ensure smooth communication as the serious AEFI is being investigated and causality assessment done. [12]

reporting suspected cases of COVID-19 vaccine failure and also serious AEFI. They are central to the expansion of knowledge about the effectiveness and safety of the COVID-19 vaccines post-licensure. Each country needs to share their findings so global assessment of the effectiveness of the different COVID-19 vaccines in different settings can be known. The serious adverse events assessed by the causality assessment committee to be linked to the vaccine, its manufacture, an immunization program error or to an immunization stress related response[13] all need to be reported to the Uppsala Monitoring Centre, part of the World Health Organization Programme for International Drug Monitoring including for vaccines (https://www.who-umc.org/).

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What is meant by benefit-risk assessment of the vaccine in high priority populations?

Sonali Kochhar and Q&A Team

Vaccination is one of the most successful public health interventions for disease

very low. It is essential that vaccines have a highly favorable benefit-risk balance i.e. the benefits of vaccination must be significantly greater when compared to any risk of harm. This ensures appropriate and informed public health decision making.[2]

Benefit-risk assessment is the basis of regulatory decisions for all vaccines and drugs during the pre and post licensure review processes.[2,3] Authorization for a vaccine or drug use is granted only if the benefit-risk assessment shows a sufficient positive benefit-risk balance based on the scientific evidence.[3]

The benefit-risk assessment of a vaccine or drug might be different for specific populations (e.g., children, pregnant women, and immunocompromised people), and for people at high versus low risk of disease (e.g, living in an area with an active outbreak).[3]

The benefit-risk assessment takes into consideration a number of factors including the severity of the disease, how well currently available medicines for the disease address the population's medical needs, the effectiveness of the vaccine in preventing disease in specific populations, and the risk of adverse events following vaccination in the same populations compared with the risk associated with the disease.[2,3,4]

As an **example for measles vaccine**, the benefit of vaccines far outweighs the risks (the risk of adverse events following vaccination needs to be compared with the risk associated with the disease. The risk of side-effects of the treatment used to alleviate the symptoms of the disease are also taken into account).[5]

Benefit-Risk Assessment of Measles vaccine[5]
(Risk of adverse events following vaccination compared with the risk associated with the disease and risk of side-effects of the treatment used to alleviate the symptoms of the disease)

Vaccine Possible unwanted side effects of measles vaccine	Disease Possible complications of the disease and possible side effects of its treatment	Treatment Possible side-effects of its treatment
Very Common Mild, local reactions, such as redness and pain at the injection site, occur in more than 10% of vaccinations	**Otitis (Ear Infection)** 7-9% of infected people	**Common** (One or more of the following occurs in 1-9% of people who use the drug): - Irritation and inflammation inside the nose (rhinitis) - Severe shortness of breath (dyspnea) - Coughing, heaviness and tightness in the chest or wheezing (paroxysmal bronchial spasm) - Bleeding from the gastrointestinal digestive tract (gastrointestinal haemorrhage) - Indigestion or upset stomach (dyspepsia) - Abdominal pain - Ulcer - Other
Common Fever occurs in 5-10% of vaccinations, Rash occurs in 5% of vaccinations	**Diarrhea** 6% of infected people	**In Addition** - Liver and kidney damage may occur in case of an overdose - Serious complications may occur in combination with other drugs
Rare Fever with convulsions occur in less than 0.1% of vaccinations	**Chronic and progressive Brain Inflammation (SSPE)** 1 out of every 100 000 infected people	
Very rare - Inflammation of brain and spinal cord (encephalomyelitis) occurs in 1 out of 1 million vaccinations - Low blood platelet count (thrombocytopenia) occurs in 1 out of 30 000-	**Pneumonia** 1-6% of infected people	

3.5 out of 10 million vaccinations		
	Infection that causes Brain Swelling (Encephalomyelitis) 1 out of every 2000 infected people	
	Death 0.1-1 out of every 1000 infected people	

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What are the common side effects expected with the vaccines?

Youngmee Jee and Q&A Team

happen after vaccination that might be coincidental or related to the vaccine.

We do not yet have enough trial data to say what will be the minor and serious adverse events with the new COVID-19 vaccines. However, we do know about adverse events with other types of injectable vaccines.

- Minor common side effects can be pain at injection site, redness/ swelling at injection site, low-grade fever, fatigue, headache, and minor muscle and/or joint pain (see Table 1).[1] Usually these minor side effects occur within a few hours of injection but will go away within a few days.
- Severe side effects such as seizures, thrombocytopenia, prolonged crying can occur rarely but usually do not result in long term problems.[1]
- Allergic reactions such as anaphylaxis are very rare but can occur immediately (usually within minutes) after vaccination (e.g., due to a vaccine component such as neomycin) and can be life-threatening. Healthcare providers should be prepared to treat the symptoms of anaphylaxis.[1]
- Vaccine adverse events can be classified into 5 categories:
    1. vaccine product-related reaction,
    2. vaccine quality detect-related reaction,
    3. immunization error-related reaction,
    4. immunization stress-related reaction and
    5. coincidental event.[1]
- Adverse events following immunization is considered serious if it results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, persistent or significant disability/incapacity, is a congenital anomaly/birth defect or requires intervention to prevent impairment of damage. Expected rates of AEFI following some childhood vaccines are provided at https://vaccine-safety-training.org/.[1]
- Safety data from phase III trials of Pfizer COVID-19 vaccine[2] showed common side effects such as headache, chills, joint pain, diarrhea and chills were less among older age groups than younger age groups. Most side effects after the

- The Moderna COVID-19 vaccine's reported safety profile[3] also showed minor common side effects. Of note, systemic adverse events were more common following the second dose and in those receiving the highest dose.
- COVID-19 vaccines that complete phase 3 trials having been administered to 20,000 individuals or more with very few or no serious adverse effects and are shown to be efficacious are likely to receive regulatory approval for use.[4]

Table 1. Common, minor vaccine reactions and treatment

Vaccine	Local reactions (pain, swelling, redness)	Systemic reactions: Fever > 38°C	Systemic reactions: Irritability, malaise and systemic symptoms
Treatment	• Cold cloth at injection site • Paracetamol[6]	• Give extra oral fluids • Wear cool clothing • Tepid sponge or bath • Paracetamol[6]	• Give extra oral fluids
BCG[1]	90 – 95%	–	–
Hepatitis B	Adults up to 15% Children up to 5%	1 – 6%	–
Hib	5 – 15%	2 – 10%	–
Measles/MR/MMR	~ 10%	5 – 15%	5% (Rash)
OPV	None	Less than 1%	Less than 1%[2]
Pertussis (DTwP)	up to 50%	up to 50%	up to 55%
Pneumococcal conjugate[5]	~ 20%	~ 20%	~ 20%
Tetanus/DT/aTd	10%[4]	10%	23%

1. Local reactogenicity varies from one vaccine brand to another, depending on the strain and the number of viable antigen in the vaccine.
2. Diarrhoea, headache and/or muscle pains.
3. When compared with whole cell pertussis (DTwP) vaccine, acellular pertussis (DTaP) vaccine rates are lower.
4. Rate of local reactions are likely to increase with booster doses, up to 50 – 85%.
5. Source: http://www.cdc.gov/vaccines/hcp/acip-recs/
6. Paracetamol dose: up to 15mg/kg every 6–8 hours, maximum of 4 doses in 24 hours.

Source: WHO Vaccine safety basics e-learning course (module 3: Adverse events following immunization)

Tetanus/DT/aTd	~ 10%[4]	~ 10%	~ 25%

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What will be the measures taken if a vaccine recipient experiences a side effect?

Noni MacDonald and Q&A Panel

Side effects are called adverse events – and those following immunization, Adverse Events Following Immunization (AEFI).
"Any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease."[1]

Common, minor AEFIs with different types of immunizations including signs and symptoms such as low grade fever, muscle pain, body ache, local pain, redness and/or swelling at the injection site, usually occur in less than 20% of the vaccine recipients within a few hours of the injection, resolve after a short period of time and have no long term consequences. With any new vaccine such as the COVID-19

age groups or in those with different underlying conditions, i.e. information that might not be available from the trials.

The intensity of the AEFI will be generally mild and can very rarely be moderate or severe (e.g. mild or moderate fever). Severe AEFI do not necessarily lead to long term problems.[1]

The AEFI that should draw attention quickly are “serious” AEFI.
“A serious AEFI is one that results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or requires intervention to prevent permanent impairment or damage.”[1]

Serious AEFI are usually not detected in the clinical trials because they are very rare, i.e. occur in less than 1 in 10,000 vaccine recipients. The critical point with serious AEFI, is to determine if the AEFI is due to the vaccine itself i.e. vaccine product-related reaction; is a vaccine quality defect-related reaction i.e. a vaccine manufacturing problem; is a program error; an immunization error-related reaction i.e. a program error such as improper vaccine storage, wrong diluent used etc.; an immunization stress-related reaction i.e. a coincidental event.[1,2]

Often events are coincidental. Note if the serious AEFI is indeed vaccine related, corrective action i.e. recalling the vaccine may occur. However, due to the rigor of the prevaccine approval process, the rigor of the approval process as well as the high quality of manufacturing, rarely is the vaccine the problem in a serious AEFI.

Health care workers have several very important roles in relation to AEFI.
a) Recognize and report serious AEFI and if requested also minor AEFI;
b) Provide care to the patient with the AEFI;
c) Help gather the case information that the Causality Assessment Committee will need to determine if the serious AEFI is vaccine related or not;[3]
d) Remain objective in reaching any conclusion about the cause of the AEFI.
e) Communicate in an effective, timely and respectful manner, grounded in the known facts of the event. The local public health programme should also be prepared to communicate on the event and steps being taken to investigate and

misinformation.

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For a two dose vaccine, are there any safety considerations if the second dose of the vaccine is replaced by another vaccine?

Sonali Kochhar and Q&A Team

There are no data from the clinical trials to support the second dose of the vaccine being replaced by another COVID19 vaccine. It is recommended that the vaccine details are confirmed before immunization to ensure the correct vaccine product is given.

Should pregnant women receive the vaccine?

Sonali Kochhar and Q&A Team

pregnancy and birth outcomes as well. To date, there are no data regarding whether COVID-19 vaccines are safe or effective in pregnant women as they have been excluded from clinical trials. It is important that data specific to pregnant women are generated from their inclusion in later stage clinical trials, pregnancy-specific safety studies and follow up of trial participants who inadvertently become pregnant during Phase III clinical trials to inform public health recommendations for COVID vaccine use in this population.[3,4]

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Long term effects of vaccines

How will we know if a vaccine has long term safety concerns?

Karina Top and Q&A Team

and effectiveness after introduction into the population. At a minimum, countries are recommended to implement passive surveillance systems that collect individual reports of adverse events following immunization from healthcare providers, vaccine manufacturers and often the public.[1] These reports are collated and analyzed to identify any patterns that may suggest a safety concern with the vaccine (e.g., a certain condition reported more often after a specific vaccine than expected based on the background rate of that condition in the population). Countries that have the capacity are also recommended to institute active surveillance systems that search for cases of adverse events of special importance (e.g., seizures, Guillain Barré Syndrome) after immunization and compare rates of those conditions among vaccinated and unvaccinated groups to determine if the adverse events occurred by chance (which is commonly seen) or were related to the vaccine.

As done for any new vaccine, passive and active surveillance systems will be enhanced to identify specific adverse events of special importance following COVID-19 vaccines in a timely fashion. National and international public health organizations are already working to develop guidelines and strategies to ensure robust post-market safety monitoring of COVID-19 vaccines. The World Health Organization's Global Advisory Committee on Vaccine Safety and the Brighton Collaboration, an international consortium of vaccine safety experts, in collaboration with the Coalition for Epidemic Preparedness Innovations (CEPI) are developing guidelines and case definitions for monitoring the safety of COVID-19 vaccines (expected to be available online December 2020).[2]

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