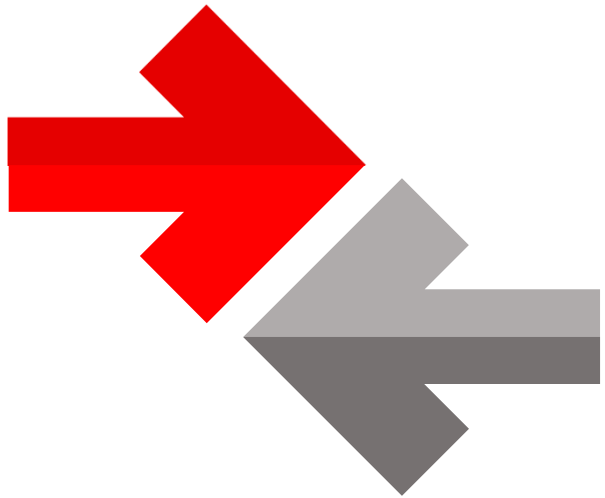
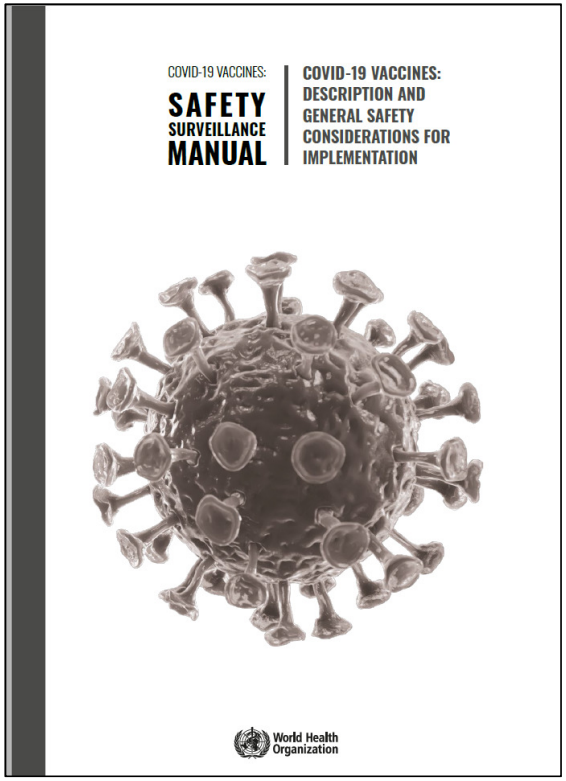
COVID-19 vaccines: Description and general safety considerations for implementation





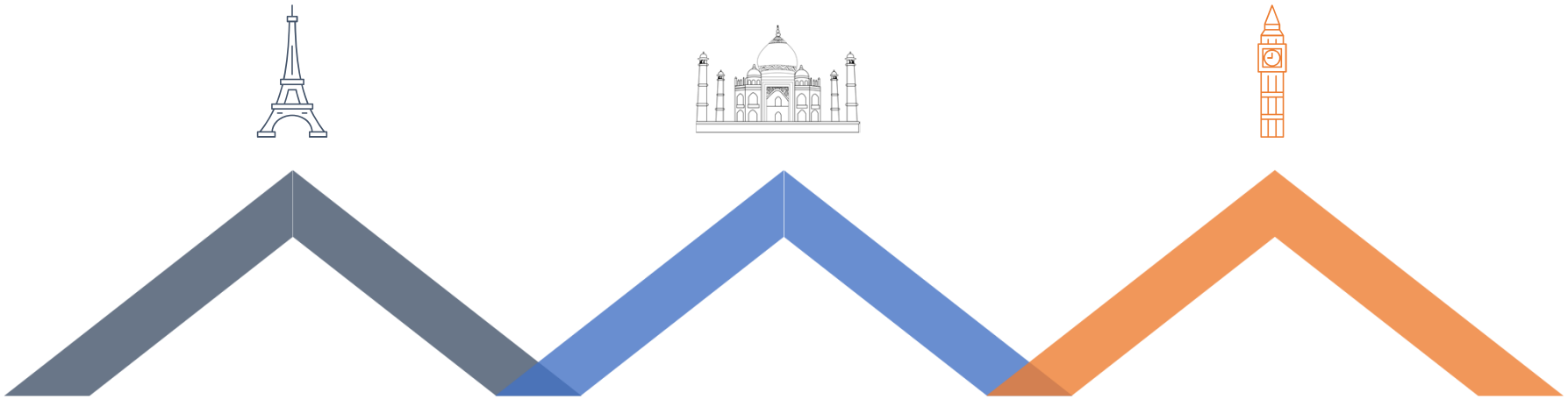
Learning objectives: The learner will be able to

Compare the general safety concerns for various vaccine platforms

Discuss the safety implications for vaccination in specific situations

Distinguish vaccine safety considerations for different vaccination strategies

Presentation structure



The current vaccine landscape and the safety profile of the various platforms

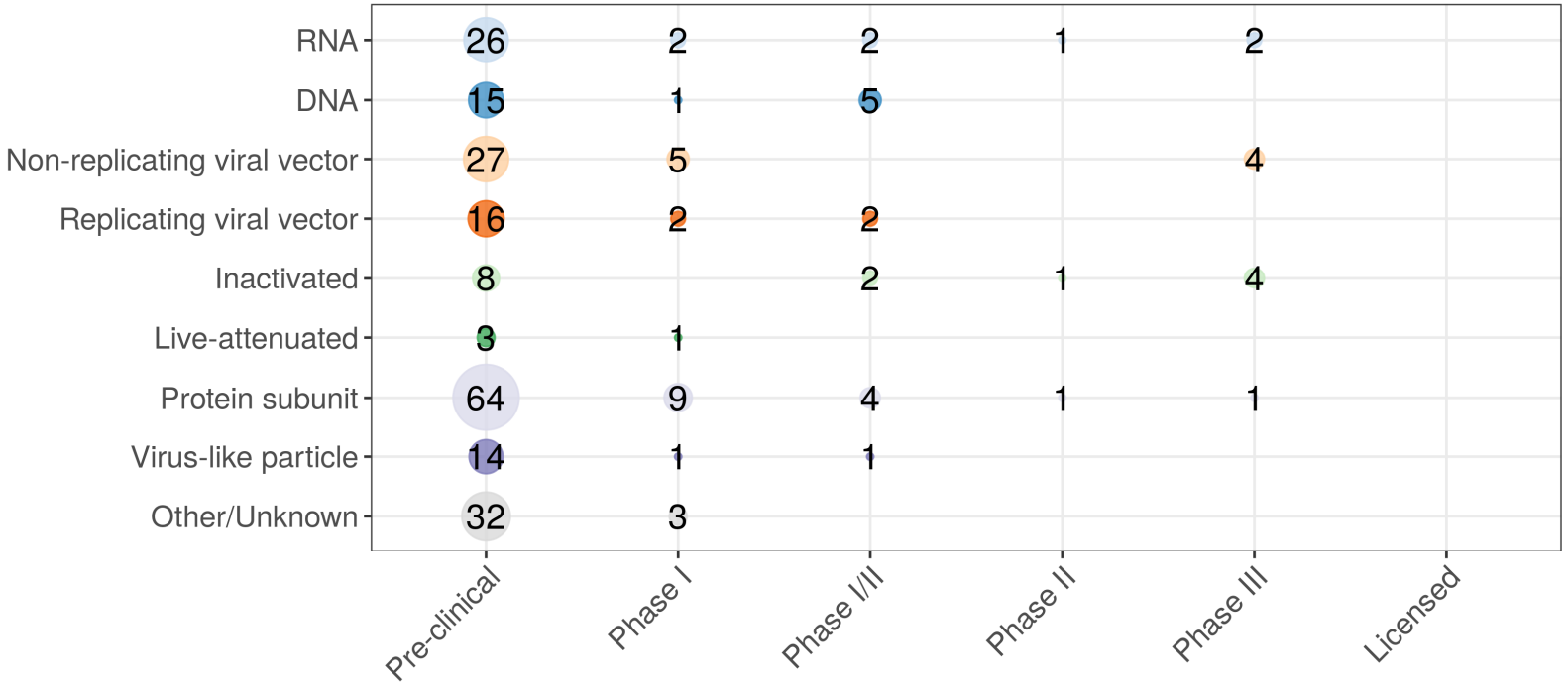
Safety implications for implementing COVID-19 Vaccination for target populations

Vaccination strategies and vaccine safety

Current status of vaccine development* (11 Nov 2020)

259 vaccine candidates

54 in clinical testing



*London School of Hygiene and Tropical Medicine: https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

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Characteristics and safety profile of COVID-19 vaccine candidates

All COVID-19 vaccines are novel vaccines that have never been used in humans on a large scale

Dossiers with safety data submitted to national regulatory authorities should be carefully assessed before the vaccine is licensed for use

The number of individuals exposed during clinical trials is limited and the profile of the clinical trial participants does not represent the broader spectrum of individuals who will be the actual vaccine recipients

All information that is currently available is from clinical trials provided by the vaccine manufacturers.

Rare AEFIs, particularly those that are unique to specific populations will be unknown when the COVID-19 vaccines are licenced.

It is strongly recommended that high quality national or regional surveillance systems capable of identifying both known AEFIs seen in clinical trials and potential rare adverse events are implemented to identify any safety issues.

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General safety considerations - Inactivated viral vaccines

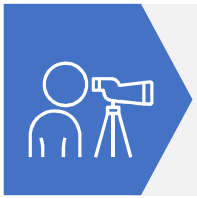
Incomplete inactivation of viral particles causing the vaccine to retain virulence and cause disease

Development of vaccine-associated enhanced disease (VAED) when vaccinated individuals encounter the pathogen later.

Adverse events caused by vaccine additives used (e.g. adjuvants)

General safety considerations - Live-attenuated viral vaccines

As of October 2020, four vaccine candidates generated by a genetic process called codon deoptimization, are in the preclinical phase.



Codon deoptimization involves replacement of commonly used codons with nonpreferred codons, which can dramatically decrease gene expression.

These candidate vaccines are based on attenuated versions of the wild type SARS-CoV-2 virus.

One inherent problem of live-attenuated vaccines is that they can revert to the virulent strain but usually more than one mutation is introduced and, therefore, the risk is considerably minimized.

General safety considerations -Viral vector based vaccines

Such vaccines are developed by introducing the genetic sequence coding for the antigen from the pathogen into a viral vector that has been previously rendered non-virulent by genetic techniques.

Some such viral vector vaccines can replicate in the host cell (eg Ebola vaccine) and some vectors don't (non-replicating viral vector vaccines)

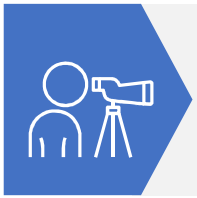
Potential risks depend on their main components, the biology of the source virus, the pre-existence of anti-vector immunity, its wild-type behaviour, pathogenesis and behaviour of the genetically modified version (the vector) and the immunogenicity and pathogenesis of the specific vaccine.

A theoretical risk of mutagenesis due to DNA integration into the host genome exists, as well as a potentially very low risk of return to virulence of the vector.

Vaccine failure is also possible

General safety considerations - Protein-based vaccines

The surface spike protein from the SARS-CoV-2 virus is the main target for this approach.



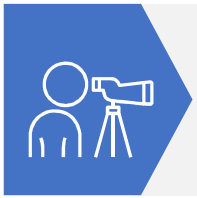
Candidate vaccines have different molecular structures for the antigenic protein, use different adjuvants and are produced using different processes to enhance their efficacy.

Virus-like particles (VLP) are empty virus shells that mimic the wild virus structure but are not infectious as they contain no genetic material

The risks depend on the type of protein used (e.g. Protein S, M or N, dimeric, monomeric), the type of immune response (e.g. Th1/2), the production system and also the final composition of the vaccine (i.e. adjuvants, stabilizers)

General safety considerations - Nucleic acid vaccines

AEFI could be related to nucleotide sequence of the antigenic gene, the surrounding sequences or promoters, the source of the plasmid and the nature of the microorganism and its origin.



The main theoretical risks are immune-mediated events, local and systemic reactions due to pro-inflammatory properties of the plasmids carrying the DNA sequence or of mRNA segment.

mRNA vaccines: Have the potential for integration into host cell this is not proven so far, mRNA has been proven to be stimulate innate immunity, therefore immune-mediated adverse events are also possible.

DNA vaccines: The integration of the DNA into the host cells' DNA is a potential risk but none of the human or animal studies have shown integration

Safety implications for implementing COVID-19 Vaccination for priority target populations

WHY

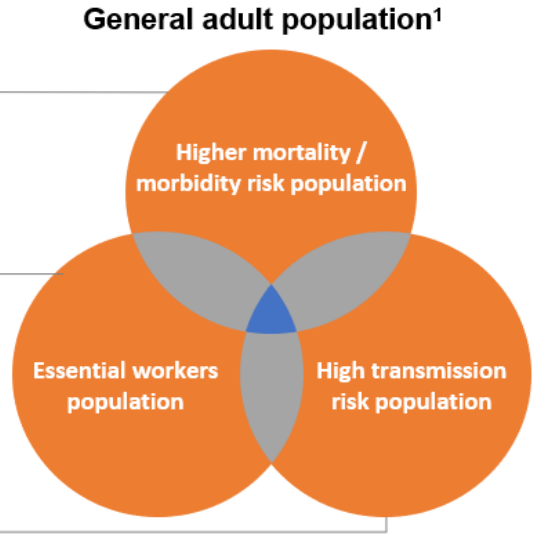
Priority populations are defined by the rationale for their vaccinations i.e., why would you want to vaccinate this population?

Priority populations

Population with higher mortality and serious morbidity rates than general population where risk-benefit analysis warrant vaccination

Individuals who provide critical societal goods and services

Individuals who are more likely to be exposed and spread the virus e.g., those exposed to super-spreader events



Vaccines should also be prioritized / reserved for disease outbreaks

1. Non-adult populations require further consideration

WHO

Target groups are who you would want to vaccinate and are defined by a common characteristic (e.g., age, health status, occupation) which allows you to identify them

Examples of potential target groups

(ordering does not imply sequencing or prioritization)

- Elderly (>65 years)
- Workers in health and social care settings
- <65 with co-morbidities
- Other essential workers
- Adults in densely populated areas
- Rest of adult population

Safety implications in priority target populations

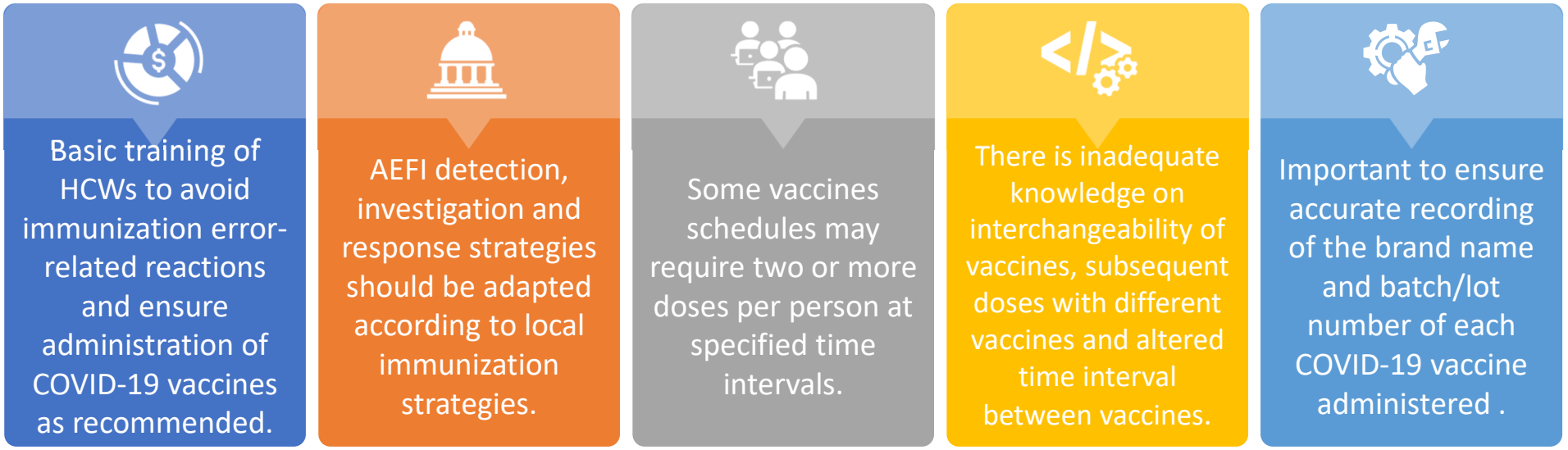
Clinics or settings that care for adults may not be familiar with AEFI reporting processes as vaccination focuses on children and pregnant women currently.

Adults, especially the elderly, have more comorbid conditions than children and, therefore a higher incidence of coincidental AEFIs should be anticipated.

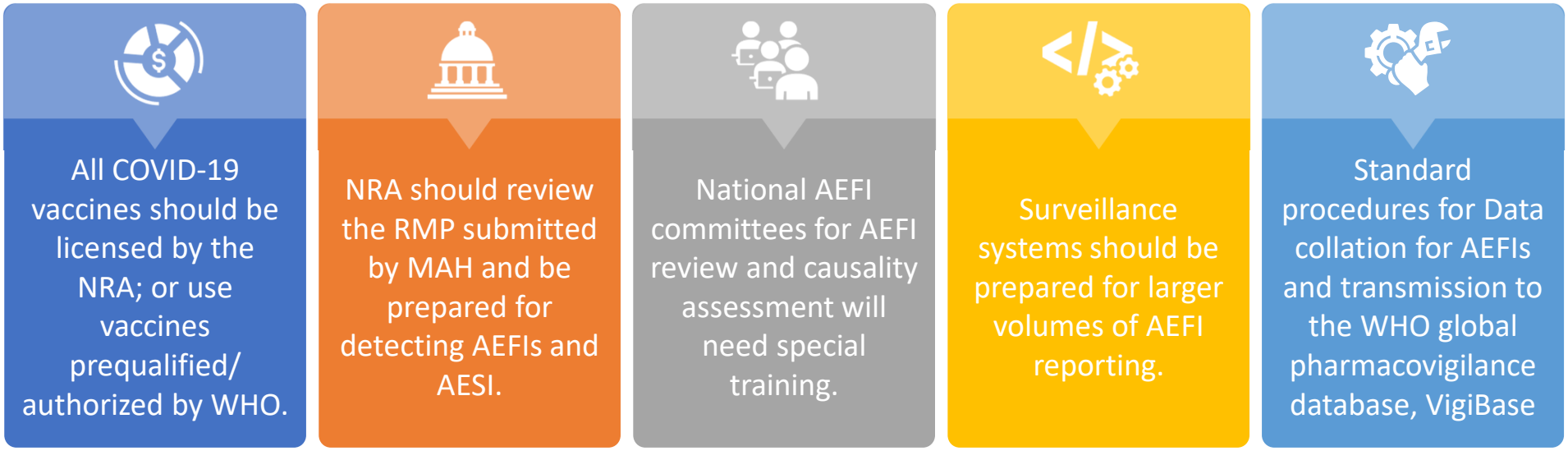
COVID-19 vaccine interactions with medications, other vaccines and other products are currently unknown

Vaccinees in the reproductive age group may be unaware of their pregnancy status when they receive the vaccine.

Safety implications for immunization programmes



Safety implication for vaccine pharmacovigilance



Broad safety considerations for COVID-19 vaccine administration in mass immunization campaigns

1. **Training on vaccination including infection prevention measures**
2. **Personal protective equipment usage for HCWs**
3. **Size and characteristics of the target population and managing sessions**
4. **Planning strategies based on goal of immunization in priority target population**
5. **Period of time for deployment and vaccination**
6. **Standard operating procedures (SOPs) and training for the management of possible AEFI**
7. **Additional human and financial resources needed**
8. **Joint health information system for reporting vaccination coverage and AEFI reporting**
9. **Rapid response teams for responding to vaccination emergencies, conducting AEFI investigations and crisis management.**

Common safety issues in mass campaigns

Increase in immunization errors

Staff may have less experience with adverse events (e.g. fainting with older children)

Rumours jeopardize justification of campaign.

If not dealt with immediately, rumours may not be countered sufficiently.

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Safety considerations at the time of COVID-19 vaccine administration

1. **Before vaccinating, HCWs should verify the product on vaccine and diluent labels, check for vaccine contraindications, as indicated in the product information leaflet.**

2. **A clear interpersonal communication with the vaccinee prior to vaccination to ensure the right safety messages are communicated prior to, during and after vaccination**

3. **Advise on what should be done should any serious AEFIs occur.**

Key points to remember

- Each COVID-19 vaccine platform has its own unique safety profile

- Vaccine safety should consider the overall vaccination strategy as well as the target population

- A good knowledge of the safety profile of the vaccine and communicating the same to the beneficiary are key to prevent, identify and respond to potential safety challenges that may arise.

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