Vigilance in vaccines

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MASTER'S DEGREE PROGRAM
"DEVELOPMENT OF NEW MEDICINES-RESEARCH, MARKETING AND ACCESS"

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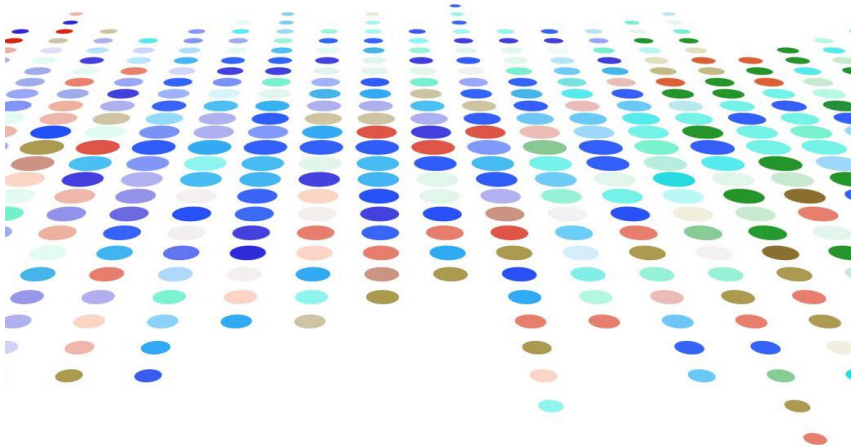
Introduction to Vigilance & Vaccinovigilance



Monitoring for: Adverse Events (or Reactions) Following Immunization (AEFI)

Vaccines' safety is first evaluated throughout clinical development and again after licensing

Vigilance evaluations will define whether a vaccine will continue its commercialisation

Vaccines safety profile: compares favorably with that of other pharmaceutical products but comes with additional challenges

Vaccines VS Medicines

Defining the threshold of accepted risks

Target population

- Healthy individuals
- Paediatric & vulnerable populations

Population coverage

- Large fractions of the population and affecting so many individuals

Regional considerations

- Disease characteristics
- Vaccine coverage
- Community immunity
- Disease severity
- Proportion of infected persons with a clinical disease (e.g., rotavirus vaccine & intussusception)

Vaccines VS Medicines

Aspects to consider

Complexity of molecules

- Safety profile: active antigens, excipients and adjuvants
- Different types of vaccines (live attenuated, mRNA, toxoids, viral vectors)

Biological aspects

- Inherent variability
- Importance of tracing

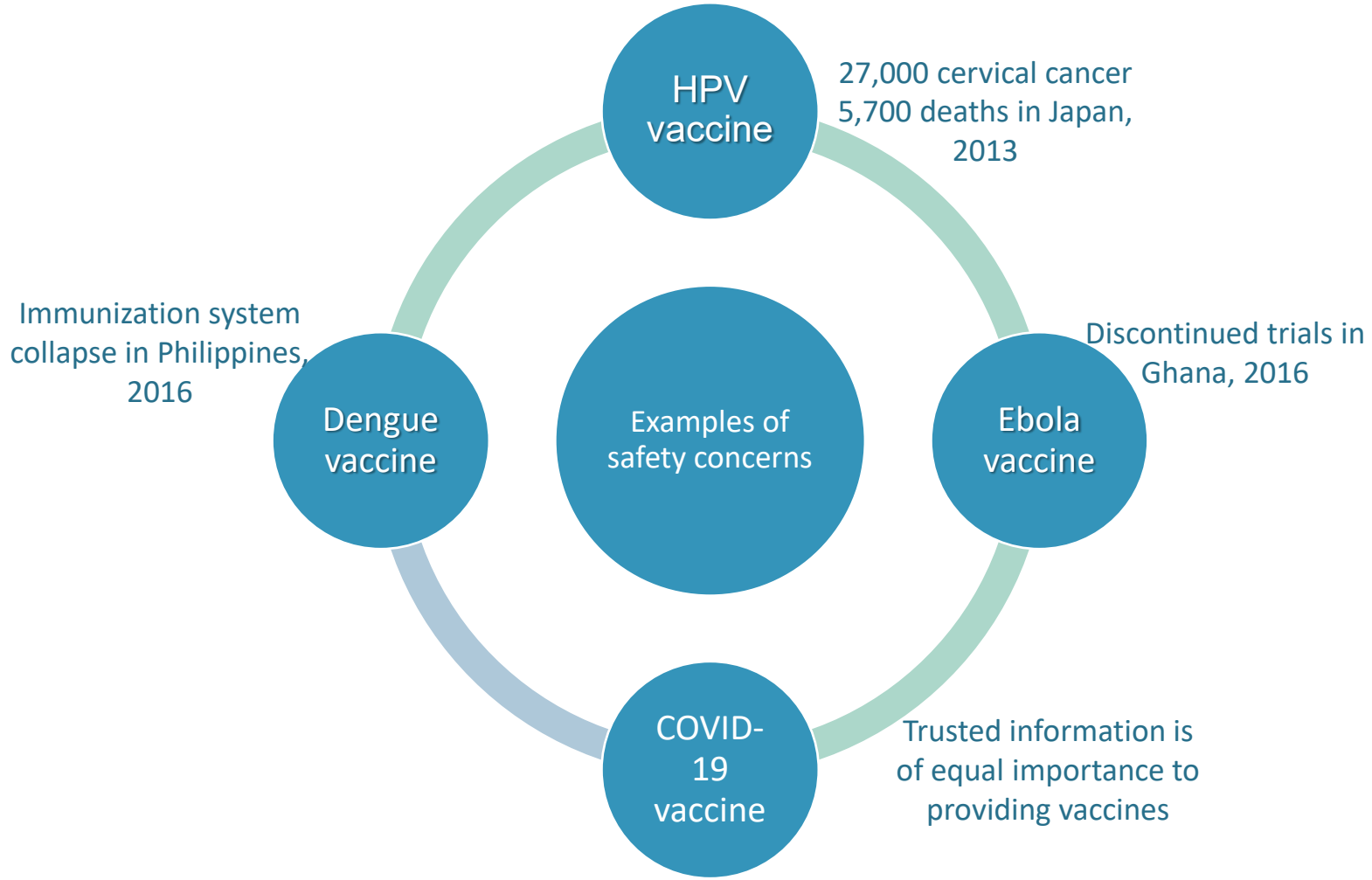
Dynamic risk-benefit ratio

- Vaccine success → reduction of targeted disease incidents

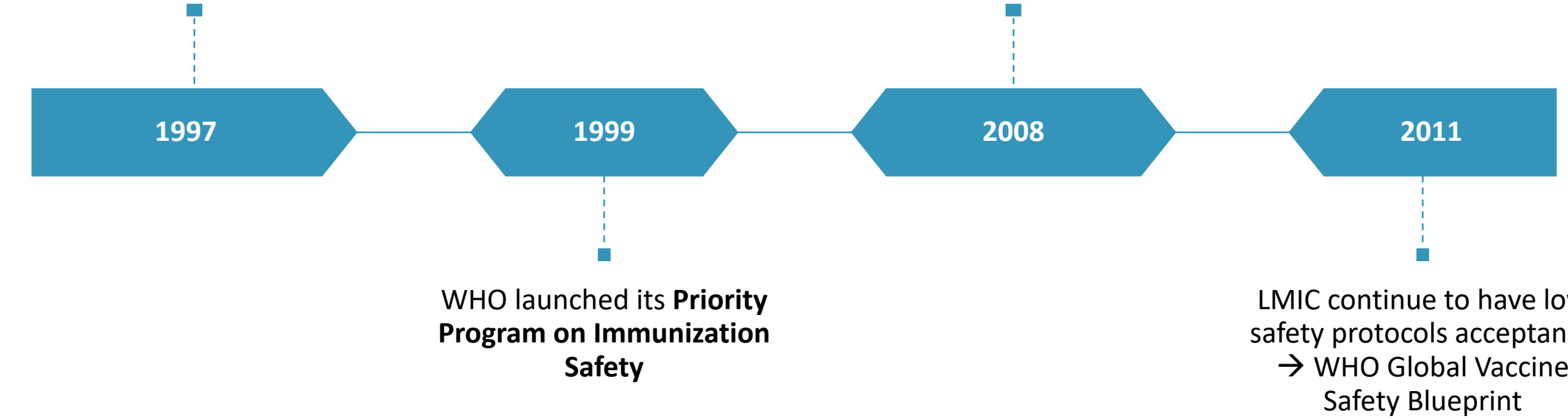
Vaccines VS Medicines

Risk communication & public opinion

In 2019, "Vaccine Hesitancy" was named by the WHO as one of the top 10 threats to global health



Safety system for vaccines: **Reliable NRAs**



Global indicator for vaccine safety

Countries heterogeneity in safety reporting

(sizeable percentage of countries reporting no events at all)

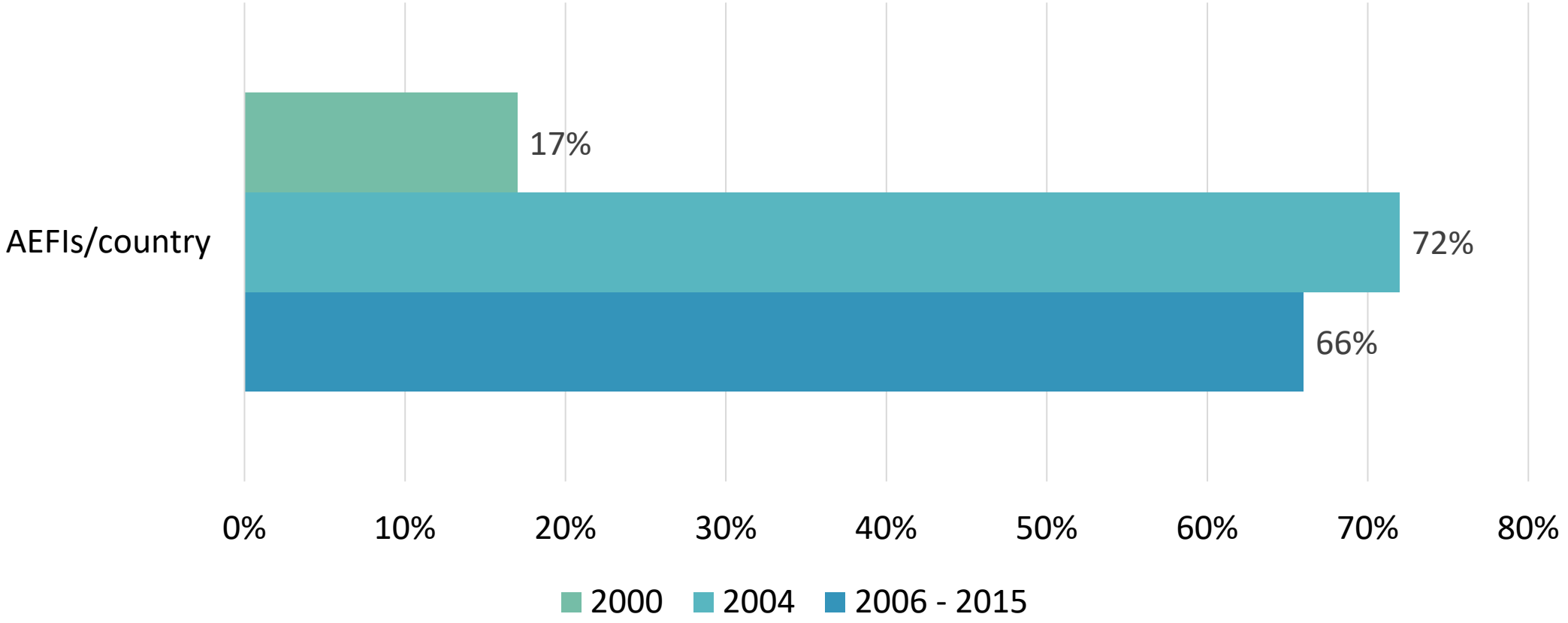
Performance measure:

The frequency of safety reports per 100,000 live births

Current goal for a viable passive immunization safety surveillance system → at least 10 reports per 100,000 live neonates annually

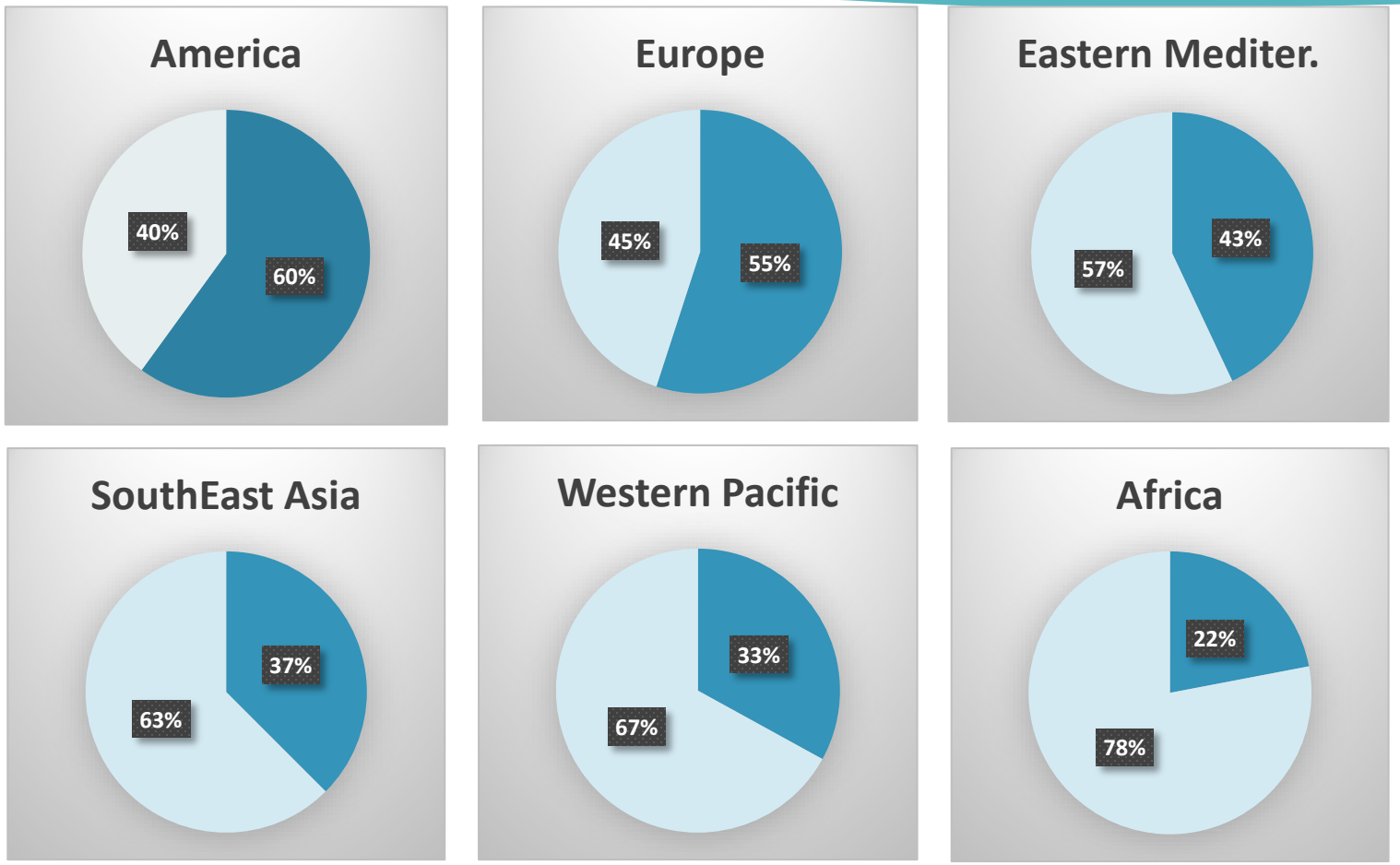
Global indicator for vaccine safety

Countries reaching the goal



Global indicator for vaccine safety

In 2015, the reporting goal was reached:



2021 WHO recommendations

- New indicator for all age groups (AEFIs / 1,000.000 population in a year)
- New target for seriousness (minimum 1 SAEFI / 1,000.000 population in a year)

The future

Need for further research into new vaccines, with more complex technologies

Continuous re-evaluation and adaptation of monitoring systems

Transparent and reliable communication channels

Critical to establish international cooperation and harmonisation

THANK YOU FOR YOUR ATTENTION

BACK UP SLIDES

Safety system for vaccines: **Challenges in LMICs**

DATA COLLECTION DIFFICULTIES

Vaccination locations far apart, resulting in a high rate of lost patients

Issues with undiscovered comorbidities

Limitations of data collecting and management systems

lack of a culture of monitoring safety as a quality process for the program. There may be a "culture of fear" in which health personnel in some countries are afraid to report AEFI for fear of being judged or punished

IMPORTANCE OF LMICs

Around twice as many vaccine doses are administered in LMICs as in developed nations due to advances in vaccination coverage and the addition of vaccines to national immunization programs in recent years.

New vaccines to be developed, marketed, and exported from LMICs.

Increasing number of high-quality vaccine producers and functional regulatory

Success of strategies like product development partnerships

Need for a harmonized global vaccination safety system to control, lead and institutionally support the NRA's vigilance activities across LMICs & HICs

Death as a consequence of immunization

Vaccination quality issues have resulted in deaths on rare occasions throughout history, typically as a result of only partial inactivation of a live vaccine.

- The BCG vaccine used in the German city of Lübeck in 1929 was contaminated with a live strain of human tuberculosis, killing 72 of the 252 children who received the vaccine.
- In 1955, the United States saw 56 cases of paralytic poliomyelitis and 5 deaths due to insufficient activation of oral polio vaccination in the Cutter event

- Good Manufacturing Practice (GMP) framework now governs vaccine quality control, and thorough batch-to-batch testing and batch release ensure measures are in place to prohibit the use of vaccinations with substantial quality problems
- no deaths attributed to manufacturing flaws in the last half-century

Toxic shock syndrome (TSS) and death can result from a vaccination vial being contaminated with microorganisms (often Staphylococcus aureus) due to carelessness (145). In fact, this is among the most prevalent adverse reactions to vaccines and a leading cause of death. Vial sterility is crucial for the prevention of TSS, hence the cold chain and multidose procedures must be strictly adhered to.

Anxiety-related reactions - The EMA guidance highlights the importance of their prevention

- There have been reports of trauma caused by syncope, most typically after HPV vaccine in adolescent females, and one death has been connected to trauma caused by a vaso-paracolic syncope after vaccination (147)
- Canadian guidance: Increasing muscle tension, such as by squeezing a rubber ball at the moment of injection, may avoid angio-paracolic syncope in patients older than 7 years old

More fatalities will likely be reported as AEFIs as vaccine safety surveillance systems in LMIC are improved, as seen in the WHO South-East Asia region (130). With very few cases, vaccines do not cause fatalities (anaphylaxis, visceral disease, disseminated vaccine disease in the immunocompromised, or quality- or administration-related damage such as toxic shock syndrome). Therefore, an unintentional cause of death is more likely to be reported following vaccination. Maintaining public trust in vaccinations requires establishing a clear line of reasoning between a clinical cause (very probable) and a vaccine reaction (extremely unlikely). Doing so calls for a vigilant and thorough AEFI investigation, a committed staff with knowledge in vaccine safety, and a clearly-articulated communication plan, as well as a well-functioning vaccine safety surveillance system.