IAVI VACCINE LITERACY LIBRARY

2022

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Translating **science** into **global** health impact

About IAVI

IAVI is a non-profit scientific research organization dedicated to addressing urgent, unmet global health challenges including HIV, tuberculosis, and emerging infectious diseases. Its mission is to translate scientific discoveries into affordable, globally accessible public health solutions.

Acknowledgements

IAVI would like to acknowledge the contribution of Doreen Asio, Monica Bagaya, Vincent Basajja, Kundai Chinyenze, William Dekker, Evanson Gichuru, Nyokabi Jacinta, Sarah Joseph, Dagna Laufer, Sharon Lipesa, Shelly Malhotra, Miliswa Magongo, Blossom Makhubalo, Roselyn Malogo, John Mdluli, Ireen Mosweu, Juliet Mpendo, Gaudensia Mutua, Vincent Muturi-Kioi, Conwell Mwakoi, Jauhara Nanyondo, Gertrude Nanyonjo, Jacinta Nyakobi, Faith Ochieng, Fred Otieno, Daisy Ouya, Gayle Patenaude, Hilda Phiri, Lewis Schrager, Nicole Sender, Elana Van Brakel, Anja Van der Westhuizen, Kelvin Vollenhoven, Jeffery Walimbwa, Mathias Wambuzi for reviewing the content of the **IAVI Vaccine Literacy Library**.

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The text of the **IAVI Vaccine Literacy Library** may be found online at *www.iavi.org/news-resources/iavi-vaccine-literacy-library*

IAVI gratefully acknowledges the generous support provided by the following major funders

Biomedical Advanced Research and Development Authority (BARDA) | Foundation for the National Institutes of Health | National Institute of Allergy and Infectious Diseases | amfAR, The Foundation for AIDS Research | Broadway Cares/Equity Fights AIDS | Cancer Research UK | The City of New York, Economic Development Corporation | Congressionally Directed Medical Research Program (DoD) | GSK | The Hearst Foundations | Keith Haring Foundation | Merck & Co., Inc., Kenilworth, NJ, USA (known as MSD outside the USA and Canada)

And many other generous individuals and partners around the world

As of April 2022

Abbreviations

AE	Adverse event
AIDS	Acquired immunodeficiency syndrome
APC	Antigen-presenting cell
BCG	Bacillus of Calmette and Guerin
CAB	Community advisory board
CBO	Community-based organisation
CD	Cluster of differentiation
CDC	Centers for Disease Control and Prevention
CEPI	Coalition for Epidemic Preparedness Innovations
COVID-19	Coronavirus Disease 2019
CRF	Circulating recombinant forms
CTL	Cytotoxic T lymphocyte
DNA	Deoxyribonucleic acid
DOT	Directly observed therapy
EMA	European Medicines Agency
ERC	Ethics Review Committee
FDA	U.S. Food and Drug Administration
GCLP	Good Clinical Laboratory Practice
GCP	Good Clinical Practice
HIV	Human immunodeficiency virus
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
IGRA	Interferon-gamma release assays
IRB	Institutional Review Board
LASV	Lassa virus
LMIC	Low- to middle-income countries
LTBI	Latent tuberculosis infecton
MDR-TB	Multidrug-resistant tuberculosis
M.tb	Mycobacterium tuberculosis
NAT	Nucleic acid test
NGO	Non-governmental organisation
NK	Natural killer cells
NP	Nucleoprotein
NRA	National Regulatory Authority
POD	Prevention of disease
POI	Prevention of infection
POR	Prevention of reinfection
RNA	Ribonucleic acid
SAE	Serious adverse event
SAHPRA	South African Health Products Regulatory Authority
TB	Tuberculosis
TPP	Target product profile
TST	Tuberculin skin test
UNAIDS	Joint United Nations Programme on HIV/AIDS
VISP	Vaccine-induced seropositivity
VL	Viral load
VMMC	Voluntary medical male circumcision
WHO	World Health Organization
XDR-TB	Extensively drug-resistant TB

Introduction

The **IAVI Vaccine Literacy Library** contains basic information about HIV, TB, and Lassa virus vaccines, explained in simple language and in a user-friendly format. The text is divided into eight modules covering a range of topics, from basic science and clinical trials to social and ethical issues related to vaccine development and testing, as well as future access to and use of vaccines. The resource also includes a list of abbreviations used and a glossary with definitions of key terms.

Audience

The **IAVI Vaccine Literacy Library** is targeted to a broad range of stakeholders involved in HIV, TB, and Lassa virus vaccine-related work. While all the modules can be adapted for use at the local community level, they are generally written for individuals who provide education and information related to HIV, TB and Lassa virus.

Use of the IAVI Vaccine Literacy Library

The **IAVI Vaccine Literacy Library** is meant for use by individuals and organisations that are providing education and information related to HIV, TB and Lassa virus vaccine research and development.

Groups that may use this material include, but are not limited to:

- Clinical vaccine trial site staff.
- Non-Governmental Organisation (NGO) staff, to incorporate vaccine messages into their existing work.
- Medical professionals or institutions, to provide vaccine information to patients or to incorporate into advocacy efforts.
- Health Centres, to provide clients with vaccine information.
- Academic or religious leaders, to provide information and/or informed advice.
- Community Advisory Boards.

The **IAVI Vaccine Literacy Library** is designed for multiple uses to serve a variety of needs. For certain audiences, it may be used as reference information, such as background reading for training workshops. It can also be used as a reference document to develop educational materials or tools, or to incorporate vaccine information into existing tools, such as:

- Fact sheets on specific vaccine topics.
- Brochures to be given to potential vaccine trial participants.
- Informational videos to be shown in community settings.
- Street plays to be performed in community settings.
- Radio programmes.

The **IAVI Vaccine Literacy Library** can also be used directly for recruitment of trial participants or may be used to engage communities or national-level stakeholders to build understanding of and support for clinical trials and an eventual vaccine.

Using and Navigating the Core Content

The **IAVI Vaccine Literacy Library** is divided into eight modules covering a range of topics, from basic science and clinical trials to social and ethical issues related to vaccine development and testing, as well as future access and use.

Each module can be read and used as a standalone document.

Certain issues or concepts are covered in more than one module. These "cross-cutting issues" are cross referenced to other modules in capitalised text. All scientific and technical terms are defined in a comprehensive glossary that provides definitions for technical and scientific terms and expressions.

Acknowledgement of IAVI and Materials Review

As described, the **IAVI Vaccine Literacy Library** is designed primarily as a reference on HIV, TB, and Lassa virus vaccines that can be used to develop or adapt materials or messages.

If IAVI has not been involved in production of materials or tools based on the **IAVI Vaccine Literacy Library**, no review by IAVI is required. IAVI does request that appropriate acknowledgement of the **IAVI Vaccine Literacy Library** be given, but the IAVI logo should not be used.

IAVI requests that it be notified of any tools or materials produced, in order that they be added to the **IAVI Vaccine Resource Library**, which is a public resource serving the entire HIV, TB, and Lassa virus-vaccine field. Proper credit will be given for all resources included in the **IAVI Vaccine Literacy Library**.

Disclaimer

IAVI assumes no responsibility or liability for any errors or omissions in the content of the **IAVI Vaccine Literacy Library**. The information contained in this Resource Library is provided on an 'as is' basis with no guarantees of completeness, accuracy, usefulness, or timeliness.

How to Cite the IAVI Vaccine Literacy Library

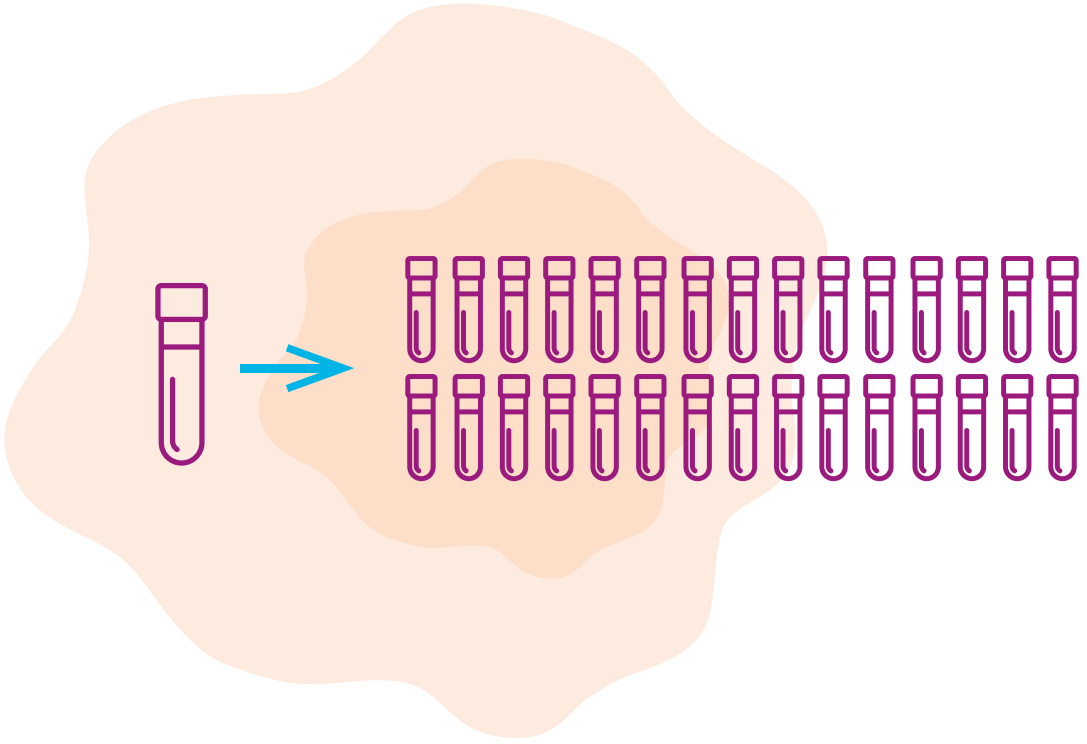
IAVI Vaccine Literacy Library, IAVI, New York, USA, 2022.

MODULE 7:
PREPARING FOR FUTURE ACCESS

MODULE 7

PREPARING FOR FUTURE ACCESS

CONTENTS 103



» Summary Points

- Making a vaccine available to the world requires much more than proving that it is safe and efficacious in clinical trials.
- There are many barriers that can prevent wide uptake and use of vaccines, including lack of funding, regulatory hurdles, manufacturing capacity, supply chain issues, affordability, and acceptability.
- Reluctance or refusal to be vaccinated (vaccine hesitancy) may be influenced by a complex mix of historical, political, social, and behavioural factors.

1. Introduction

The COVID-19 pandemic has shown that making a vaccine available to the world requires much more than proving that it is safe and efficacious in clinical trials.

Potential barriers to immediate and equitable access relate to regulatory capacity for licensure, delays in pursuing licensure in high prevalence settings, limited manufacturing capacity, ability to match demand and supply, sensible delivery systems, affordable pricing, and financing.

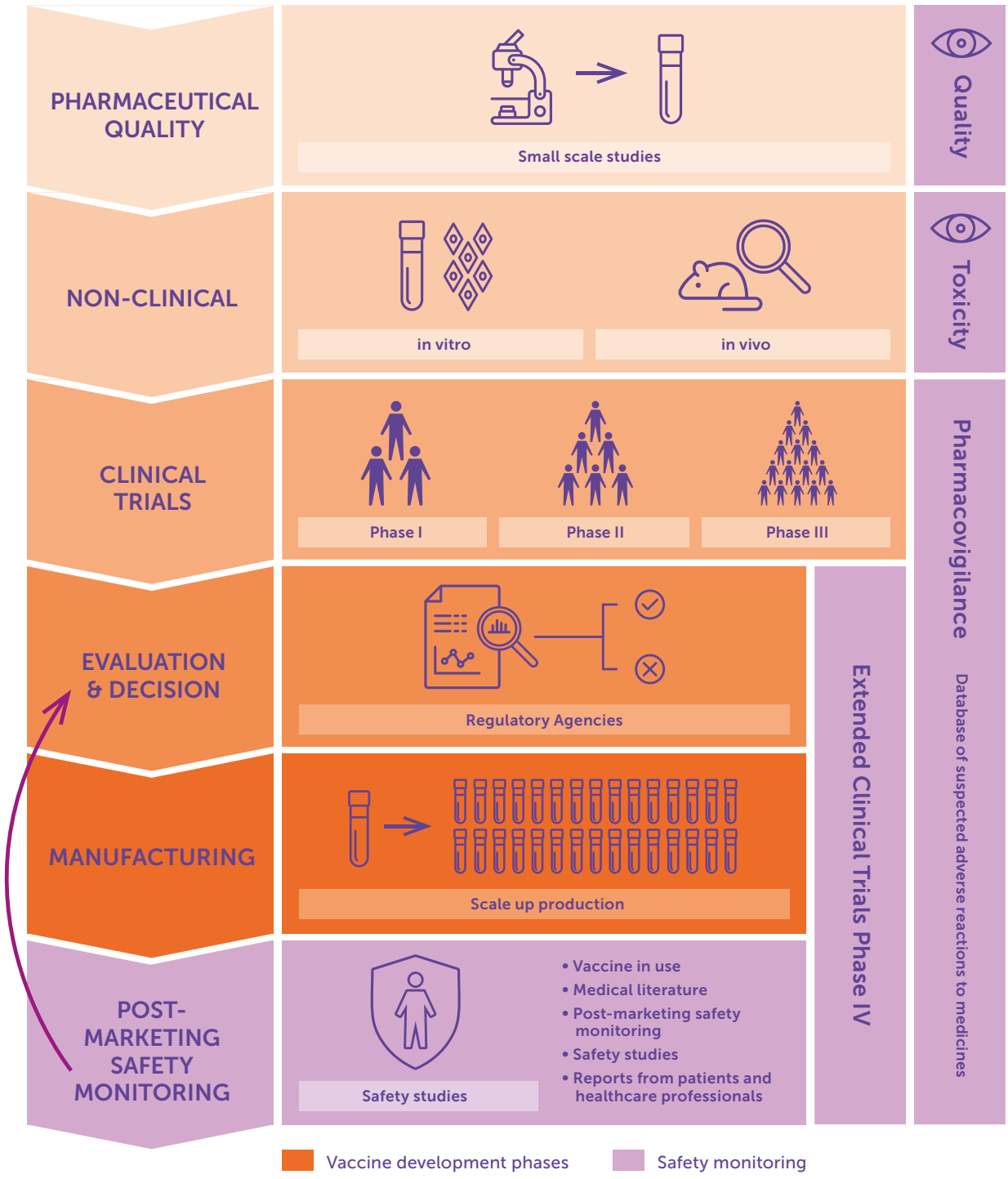
Even where these challenges are overcome, there can be low uptake of vaccines due to acceptability factors such as vaccine hesitancy, risk perception, stigma, and/or the social and political context.

Addressing the potential barriers to access during vaccine development and clinical trials can potentially make access faster once licensure has been achieved.

Vaccine development challenges

ALL VACCINES	UNIQUE TO TB AND HIV VACCINES
Manufacturing-bioprocess, formulation, and analytical development	Complex life cycle of target pathogen(s) make antigen(s) selection difficult
Optimisation of clinical immunologic assays	Protective immune response unclear
Large clinical trials required to evaluate safety in healthy individuals	Poor memory responses with rapidly waning efficacy
	Regulatory, Ethical Committee, and clinical trial infrastructure limitations for large studies involving novel technologies
	Insufficient financial resources for development
	No/limited high-income country markets

VACCINE DEVELOPMENT PHASES



2. Barriers to Vaccine Roll Out

2.1 Global Funding, Finance Mechanisms, and Pricing

Billions of dollars are needed to purchase and deliver vaccines globally. Most of this funding must come from national governments, especially in wealthy countries, as well as multinational funding bodies like Gavi, the Vaccine Alliance (Gavi), the Global Fund, and organisations like the World Bank.

Financial mechanisms must be set up to ensure that there are sufficient funds in place to purchase and deliver vaccines as soon as a product is licensed.

In addition, vaccines must be affordably priced, particularly when they have been developed with public funds. The pricing of vaccines is driven by a combination of factors but is ultimately set by the manufacturer. Some vaccines are more expensive than others to develop or produce due to their ingredients or mechanism of action.

It is possible to make vaccines available on a not-for-profit basis or have 'tiered pricing' structures to support affordability in low- and middle-income countries. The diagram below shows how COVID-19 vaccines, for example, compare in terms of price per dose.

Fifty-seven countries, many of which have high HIV prevalence, are currently eligible for financial support through Gavi for vaccine procurement. Integration of new vaccines into Gavi's Vaccine Investment Strategy, which is updated every five years, will be important for ensuring access in these low- and lower-middle income countries.

For vaccines that are procured directly from companies, the actual price that a government pays for a vaccine is negotiated with the company that produces the vaccine, depending on the number of doses ordered and the urgency of the need. A vaccine that is needed globally may be cheaper to purchase than one that is only needed in a handful of countries. Prices negotiated between vaccine makers and governments are not always made publicly available. Procuring through pooled procurement platforms, such as UNICEF or the Pan-American Health Organization (PAHO), can allow countries to access lower pricing.

Avoiding vaccine nationalism: the COVAX example

During the COVID-19 pandemic, many governments signed 'bilateral' agreements with vaccine manufacturers to supply their own populations with vaccines ahead of them becoming available for other countries.

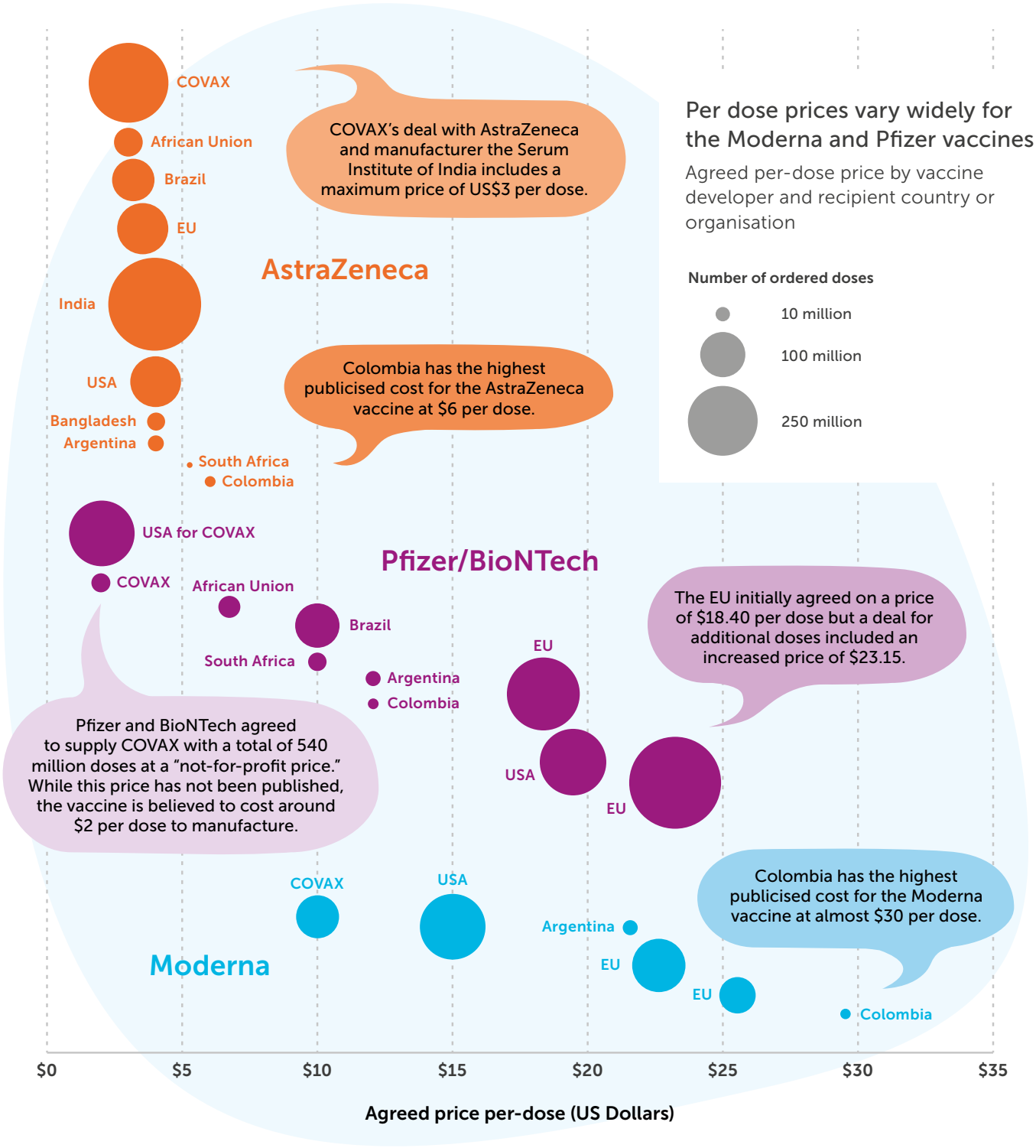
To counter this vaccine nationalism, WHO, Gavi and other global partners set up COVAX as the vaccines arm of the Access to COVID-19 Tools (ACT)-Accelerator, a ground-breaking global collaboration to accelerate development, production, and equitable access to COVID-19 tests, treatments, and vaccines.

COVAX devised centralised procurement mechanisms that enable countries to buy COVID-19 vaccines irrespective of their income status at tiered pricing levels and based on agreed upon allocation principles.

To help guarantee sufficient funding, other mechanisms for purchase and delivery can be put into place including, for example, 'advance market commitments' from funders. If such commitments are made, governments will likely be more willing and able to create systems for delivery.

Ensuring demand may also encourage investment by pharmaceutical and biotech firms who may be reluctant to invest in developing a product that might only have a small profit.

AN EXAMPLE OF VACCINE PRICING: COVID VACCINES



Source: https://www.pharmaceutical-technology.com/analysis/covid-19-vaccine-pricing-varies-country-company

2.2 Regulatory Approval and Licensure

In order to make a vaccine available in a country it must first be licensed or approved by national regulatory authorities.

Where there is a lack of regulatory expertise and capacity, countries can look to prior approval by established regulatory agencies, such as the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA). Alternatively, there are mechanisms that specifically focus on evaluating medicines intended for markets outside of the U.S. and the EU, including the EU-Medicines for all or 'EU-M4all' procedure and the WHO collaborative procedure for accelerated registration. By leveraging assessment and inspection outputs already produced by WHO prequalification, and thereby eliminating duplicative regulatory work, it speeds up in-country registration of quality-assured products and contributes to their wider availability.

Regulatory capacity in Africa has increased over time with the introduction of the African Medicines Agency and other initiatives in a growing effort to harmonise regulatory processes across the continent.

The **African Medicines Agency (AMA)** aims to establish common standards and regulations for the region, and coordinates joint reviews of clinical trial applications for vaccines.

The **East African Community's Medicines Regulatory Harmonisation** initiative supports a joint regional assessment process that harmonises technical documents, combines inspections and review processes, and accelerates approvals among member states.

The **African Vaccine Regulatory Forum (AVAREF)** assists national regulatory authorities, ethics committees, and sponsors to achieve consensus on ethical and regulatory questions surrounding the research and development of medical products in Africa. Its primary aim is to improve access to medical products across the continent by reducing review and approval times for clinical trial applications, while also optimising quality of regulatory processes.

The **South African Health Products Regulatory Authority (SAHPRA)** regulates all health products in the country through monitoring, evaluation, investigation, inspection, and registration. This includes clinical trials, complementary medicines, medical devices, and diagnostics.

Approval of a new product requires review of a detailed record that presents the safety and efficacy of the vaccine. Since the approval process and the type of data needed for approval may vary between countries, vaccine developers may be required to prepare and submit multiple applications for approval. It is important to work with regulatory authorities when designing the clinical trials to ensure that the trial will provide the necessary data to support eventual licensure. AVAREF can provide a platform for early engagement with regulators on clinical trial design.

Working with the appropriate authorities in advance may prevent unnecessary delays and assure a smoother approval process. Efforts to better coordinate and standardise regulatory processes across regions and internationally may facilitate approval.

Finally, even after vaccines have been licensed, they may not be rolled out until and unless global and national policy recommendations support their use.

2.3 Manufacturing Capacity

Manufacturing any new vaccine entails two costly elements: building large-scale manufacturing facilities and developing biological processes ('bioprocesses') to produce large quantities of the vaccine. Manufacturing vaccines is largely carried out by the private (pharmaceutical) sector.

Depending on the amount of financing available, it can take years to build sufficient capacity for manufacturing, so work should begin well in advance of vaccine availability. Advance market commitments can reduce the risk for companies when considering this.

Policy action and advocacy are needed at both the global and local level to create additional incentives for large pharmaceuticals to work on scale-up for manufacturing or to transfer their technology to other companies to do this work. Technology transfer to enable scaling up manufacturing by additional companies is often held back by issues of intellectual property.

Approaches such as voluntary licensing and early technology transfer to manufacturers with strong commercial reach in high prevalence settings could help support the scale-up of manufacturing.

2.4 Operational Research

Before making a vaccine available, a range of studies can look at how to introduce and deliver a new vaccine, including how to add it to existing prevention or other health programs. This operational research can answer questions about which vaccine delivery systems are best and how to sustain and improve on these programs as access to the new intervention expands during the rollout (program implementation) process.

2.5 Delivery and Roll Out

Vaccines for infants and children are usually integrated within newborn medical care and the school system. Unlike childhood vaccinations, the new vaccines for HIV and TB may first be available for adults who may be difficult to reach through traditional vaccine delivery systems.

Efforts to reach those who would most benefit from a vaccine may be difficult in certain settings and for certain infections. In some cases, it will be necessary to establish a 'cold-chain' to keep the vaccine at the right temperature.

Strategies for vaccine delivery should be planned ahead and placed within the broader public health agenda. They should also be compatible with existing national vaccine programmes. Important lessons can be gathered from the experience of rolling out adult and adolescent vaccines as part of the COVID-19 response.

A delivery strategy should address:

- Transportation.
- Storage facilities.
- Storage conditions.
- Appropriate venues for delivering vaccines (*e.g.*, clinics, community settings).
- Education and social marketing appropriate to specific populations.
- Human resources.
- Linkages to the wider health system.

3. Barriers to Vaccine Acceptance and Use

What makes a vaccine acceptable or not to people can depend on many factors, including:

- Actual or perceived efficacy.
- The immunisation schedule or regimen (number and timing of doses).
- Characteristics, such as method of delivery.
- Cost-effectivenes.
- Stigma and risk-perception (whether people believe they are at risk of an infection).

The acceptability of a new vaccine is important on various levels. If it is acceptable to policymakers and other influential people, they may be more willing to approve and licence the vaccine, introduce the vaccine in-country, and integrate it as part of the national health programme.

If it is acceptable to the medical community and health organisations, they may be more willing to support and promote use of the vaccine. And if it is acceptable to individuals and communities, they may be more willing to be vaccinated. Acceptability therefore affects accessibility and uptake of a vaccine.

In addition, to make sure that vaccines are accepted, supported, and used by the public, education campaigns should build knowledge among communities and societies about the characteristics, advantages, risks, and limitations of vaccines.

3.1 Vaccine Hesitancy

As we have seen with COVID-19 vaccination roll out, fears, myths, and rumours about the vaccine have a negative impact on how many people come forward to be vaccinated. The reluctance or refusal to be vaccinated may be influenced by a complex mix of historical, political, social, and behavioural factors. Some common concerns include:

- Worry that the vaccine may cause infection.
- Concern that any illness following vaccination is due to the vaccine.
- Fear that the vaccine could cause sterility.
- Misinformation spread by social networks.
- Fear that the vaccine was developed too quickly.
- Concern that long-term side effects could appear in years to come.

In 2019, WHO listed vaccine hesitancy among the 'Top 10' threats to global health, citing its potential to undermine global efforts to eradicate polio, eliminate measles, and contain certain cancers. Knowledge of vaccines and their potential benefit will have an impact on whether governments make vaccines a public health priority. It is important that advocates, community groups, and vaccine developers increase awareness and support among government officials to help ensure vaccine access.

3.2 Efficacy

The higher the efficacy of a vaccine, the more likely it is to be acceptable to individuals, public health providers, and governments. The first HIV vaccines to be licensed and made available to the public may be of low-to-moderate efficacy in comparison to some vaccines that are available for the prevention of other diseases.

Policymakers must weigh up vaccine effectiveness against its cost compared with other interventions. It is therefore critically important that stakeholders at all levels understand the benefits of a partially efficacious vaccine. Even a vaccine with relatively low efficacy would have a significant impact on the epidemic in high incidence countries if given to a large segment of the population. Epidemiological impact modelling of vaccines at varying efficacy levels can provide useful information on the potential impact of vaccines to inform local, national, and global decisions.

3.3 Product Characteristics

The characteristics of any vaccine product are strong determinants of its acceptability to the end user. A vaccine that requires one or two doses may be more acceptable than a vaccine that requires multiple doses if the infection is perceived as more serious; an oral vaccine might be more acceptable than an injected vaccine for some people. Research is needed, both early in vaccine development and in preparation for introduction, to understand the attributes, clinical trial designs, dosing schedules, packaging, presentation, and delivery approaches that will be most acceptable to eventual providers and users. These are important to inform Target Product Profiles (see **MODULE 4**) and planning for eventual access.

3.4 Stigma and Risk Perception

As with other interventions, both stigma and perceived risk are likely to affect access to and use of vaccines.

Stigma can affect how people evaluate their risk of infection (this is known as risk perception). People often believe that only certain stigmatised groups (*e.g.*, people who are homeless, or who engage in sex work or drug use) are at risk from disease. Even if people do understand their risk of exposure and the benefits of vaccination, they might fear that they will be stigmatised or judged to be high risk if they come forward for vaccination.

In the case of vaccines for HIV and other sexually transmitted infections, women in particular might fear that they will be accused of unfaithfulness, and they might experience violence from or abandonment by partners. These issues need to be addressed within vaccine delivery plans and by working closely with communities and individuals.

FIND OUT MORE...

- Evolving access pathways for long-acting HIV prevention products (2021): *https://www.iavi.org/phocadownload/Access-pathways-for-long-acting-HIV-prevention-products.pdf*
- Advocates guide to COVID-19 vaccine access: *https://www.avac.org/resource/advocate's-guide-covid-19-vaccine-access*
- Vaccine misinformation management field guide: *https://vaccinemisinformation.guide*
- Vaccine nationalism: *https://gh.bmj.com/content/6/10/e006305*

Glossary

A

Acquired immunity: immunity that develops during a person's lifetime.

Adjuvant: a substance added to its formulation to enhance or modify the immune response to the components of the vaccine.

Adverse event: an unexpected medical problem experienced by an individual in a clinical trial. The term is used whether the effect can be attributed to the vaccine under study or something else happening during the study.

Adverse reaction (also known as adverse event or side effect): in a clinical trial, an unwanted effect detected in participants and attributed to the study vaccine.

AIDS (acquired immunodeficiency syndrome): the most advanced stage of HIV infection, characterised by a deterioration of the immune system and a susceptibility to a range of opportunistic infections and cancers.

Antibody: a protein found in the blood or bodily fluids that binds, neutralises, and helps destroy pathogens (e.g., bacteria, viruses) or toxins. Antibodies are also known as immunoglobulins. Each antibody binds specifically to the antigen that stimulated its production.

Antibody-mediated immunity: immunity that results from the activity of antibodies. Also called humoral immunity.

Antigen: any substance that stimulates the immune system to trigger an immune response.

Antigen-presenting cell (APC): B cell, macrophage, dendritic cell or other cells that ingest and process pathogens such as bacteria and viruses. An APC displays fragments of the pathogen on its surface to attract and activate the cells of the immune system that respond specifically to that antigen (see also dendritic cell; macrophage).

Antiretrovirals: drugs that reduce the ability of HIV or other types of viruses to multiply in the body.

Apoptosis: cellular suicide. A possible mechanism used by HIV to destroy cells of the immune system. HIV may cause apoptosis in both HIV-infected and HIV-uninfected immune system cells. Also known as programmed cell death.

Arm: a group of participants in a clinical trial, all of whom receive the same treatment, intervention, or placebo.

Attenuated: weakened. Attenuated viruses are often used as vaccines because they can no longer produce disease but still stimulate a strong immune response, similar to that caused by the natural virus.

B

B lymphocyte (B cell): one of the two major classes of lymphocytes, B lymphocytes are white blood cells of the immune system that are derived from the bone marrow and spleen. B cells develop into plasma cells, which produce antibodies.

Baseline: the time point in a study just before initiation of an intervention (for example vaccination). Measurements taken at later time points may be compared with those taken at baseline to determine if the intervention makes a difference.

B

Binding antibody: an antibody that attaches to part of a pathogen. Binding antibodies may or may not lead to the killing of the pathogen.

Blinded study: a clinical trial in which participants are unaware as to whether they are in the experimental or control arm of the study. See also double-blind study.

Booster: a vaccine dose given after the first dose to increase the immune response to the vaccine antigen(s). A booster may be given shortly after the first dose or much later. The vaccine given as the booster dose may or may not be the same as the primary vaccine. See also prime-boost.

Breakthrough infection: an infection that occurs during a vaccine trial conducted to prevent that infection. Such an infection is caused by exposure to the infectious agent and may occur before or after the vaccine has taken effect or all doses have been given.

C

CD: abbreviation for 'cluster of differentiation,' referring to molecules at the surface of cells that are used to identify immune cells, for example, CD4+ T cells.

CD4+ T lymphocyte: cell of the immune system that carries a molecule on its surface known as 'cluster of differentiation 4' (CD4). These cells are the primary targets of HIV. Also known as helper T cells, CD4+ T cells help orchestrate the immune response, including antibody responses as well as CTL responses (see also T cell).

CD8+ T lymphocyte: cell of the immune system that carries a molecule on its surface known as 'cluster of differentiation 8' (CD8) (see also cytotoxic T lymphocyte (CTL); T cell).

Cell-mediated immunity (cellular immune response): the immune response coordinated by T cells. This branch of the immune system targets cells infected with microorganisms such as viruses, fungi, and certain bacteria.

Challenge: in vaccine research and development, the deliberate exposure of an immunised animal to the infectious agent. Challenge experiments are never done in human HIV vaccine research.

Circulating recombinant forms (CRFs): HIV made of different subtypes of the virus that have recombined.

Clade: a group of related viruses classified according to their degree of genetic similarity. Also called a subtype or strain.

Cohort: groups of individuals who share one or more characteristics in a research study and who are followed over time. For example, a vaccine trial might include two cohorts, a group at low risk for HIV and a group at higher risk for HIV.

Complement proteins: blood proteins that play an important role in the immune response. Generally, complement proteins amplify the effects of antibodies and inflammation.

Control arm: in vaccine clinical trials, the group of participants that is not given the experimental intervention. The control arm can be given an intervention that is considered effective (the standard of prevention), a placebo, or no intervention. The control group is compared with one or more groups of participants given experimental vaccines to measure any effects of the vaccines tested as well as to measure differences in safety.

C

Core: the section of a virus that contains the genetic information and other proteins needed for a virus to replicate.

Correlates of immunity (correlates of protection): the immune responses a vaccine or natural immunity need to trigger to protect an individual from a certain infection.

Cytokine: a hormone-like protein produced by white blood cells that acts as a messenger between cells. Cytokines can stimulate or inhibit the growth and activity of various immune cells. Cytokines are essential for a coordinated immune response and can also be used as immunologic adjuvants. HIV replication is regulated by a delicate balance among cytokines.

Cytotoxic T lymphocyte (CTL): a type of immune system cell that can destroy cancer cells and cells infected with viruses, fungi, or certain bacteria. Also known as killer T cells.

D

Deletion (genetic): elimination of a gene or portion of a gene. Genetic deletion can occur naturally or in the laboratory.

Dendritic cell: antigen-presenting cell with thread-like tentacles (called dendrites) used to surround antigen, which they present to T cells.

DNA (deoxyribonucleic acid): the double-stranded, helical molecular chain found within the nucleus of each cell. DNA carries the genetic information that encodes proteins and enables cells to reproduce and perform their functions.

Dose-ranging study: a clinical trial in which two or more doses (starting at a lower dose and proceeding to higher doses) of a vaccine are tested against each other to determine which dose works best and has acceptable side effects.

Dose-response relationship: the relationship between the dose of a vaccine and an immune or physiologic response. In vaccine research, a dose-response effect means that as the dose of the vaccine increases, so does the level of the immune response.

Double-blind study: a type of clinical trial in which neither the participants nor the research team know which intervention a specific participant is receiving. This helps prevent bias or expectations from influencing the results of the study.

Data and Safety Monitoring Board (DSMB): a committee of independent clinical research experts who review data while a clinical trial is in progress. The DSMB ensures that participants are not exposed to undue (unacceptable) risk and looks for any differences in effectiveness between the experimental and control groups. The DSMB may review the data in such a way that they know which group received the vaccine and which group did not. This group may also recommend that a trial be modified or stopped if there are safety concerns or if the trial objectives have been achieved or will not be achieved. See futility.

E

Effectiveness: the measurement of how well a vaccine works to reduce infection or disease in the overall population when used in the 'real world.'

Efficacy: the measurement of how well a vaccine works at producing a desired clinical effect in optimal conditions, that is, in clinical trials.

ELISA (enzyme-linked immunoabsorbent assay): a laboratory test to detect the presence of antibodies in the blood or other body fluid.

E

Endpoint: an outcome or event used to objectively measure the effect of a drug or other intervention being studied in a clinical trial. Common endpoints include infection, severe toxicity, relief of symptoms, and improvements in quality of life.

Envelope: outer surface of a virus, also called the coat. Not all viruses have an envelope.

Enzyme: a protein produced by cells to trigger a specific chemical reaction. Enzymes are generally named by adding the ending '-ase' to the name of the substance on which the enzyme acts (for example, the HIV reverse transcriptase converts HIV RNA into viral DNA)

Epidemic: a widespread outbreak of a disease in a large number of individuals over a particular period of time either in a given area or among a specific group of people.

Epidemiology: the study of the characteristics, frequency, and distribution of diseases in human populations.

Epitope: a specific part of an antigen that stimulates specific immune responses.

Experimental arm: in a clinical trial, the group of participants given the intervention being studied. Outcomes in the experimental arm are compared with those in the control arm to determine any differences, for example, in safety and effectiveness.

F

Functional antibody: an antibody that binds to an antigen and has an effect that can be demonstrated in laboratory tests. For example, neutralising antibodies are functional antibodies that inactivate HIV or prevent it from infecting other cells.

Futility: the inability of a clinical trial to achieve its objectives. A clinical trial can be stopped when an interim analysis of the results by the DSMB suggests that it is unlikely to achieve its objective and stopping it can save resources and time that could be used on more promising research.

G

Genetic engineering: the laboratory technique of recombining genes to produce proteins used for drugs and vaccines.

Genome: the complete genetic material of an organism, including all its genes. The genomes of viruses can exist as DNA or RNA.

Glycoprotein (gp): A protein that is coated with carbohydrates (sugars).

H

Healthy participant: someone with no known significant health conditions who participates in research to test a new drug, device, or intervention. Also known as 'Clinical Research Participant.'

Helper T cell: T-cell lymphocyte bearing the CD4 marker. Helper T cells regulate the functions of other cells of the immune response.

Herd immunity: protection from an infectious disease happening when a significant percentage of a population is immune to the infection either through vaccination or immunity developed through previous infection.

Host: a plant or animal harbouring another organism.

Humoral immunity: see antibody-mediated immunity.

Hypothesis: a proposed explanation made based on limited evidence as a starting point for further investigation.

I

Immune complex: an antigen bound to its specific antibody.

Immune deficiency: a breakdown or inability of certain parts of the immune system to function, thus making a person susceptible to diseases that they would not ordinarily develop.

Immunisation: the process of inducing immunity by administering a vaccine.

Immunity: protection provided by the immune system to a specific disease. Immunity may be innate or acquired, partial or complete, specific or nonspecific, long-lasting, or temporary.

Immunocompetent: capable of developing an immune response; possessing a normal immune system.

Immunogen: a substance capable of provoking an immune response. Also called an antigen.

Immunogenicity: the ability of an antigen or vaccine to stimulate immune responses.

Immunoglobulin: a general term for antibody immunotherapy: a treatment that stimulates or modifies the body's immune response.

in vitro: an artificial environment outside a living organism (e.g., in a laboratory) used for the conduct of experimental research.

in vivo: research performed with a living organism, e.g., human or animal studies.

Incidence: the number of individuals who develop a specific disease or experience a specific health-related event during a particular period of time (such as a month or year).

Inclusion/exclusion criteria: factors used to determine whether a person is eligible (inclusion criteria) or not eligible (exclusion criteria) to participate in a clinical trial. Eligibility criteria may include disease type and stage, other medical conditions, previous treatment history, age, and gender.

Informed consent: a process between a person and a researcher to ensure that the person understands all relevant facts associated with their participation in a clinical trial. Participants into a clinical trial are required to sign an informed consent form before joining a clinical trial to show that they understand the risks and benefits of participating in the research. Informed consent includes the right to leave a clinical trial at any point during the study.

Innate immunity: immunity that is present at birth and lasts a person's entire life. Innate immunity is the first response of the body's immune system to a harmful foreign substance or pathogen.

Institutional Review Board (IRB): a committee of medical professionals, statisticians, community advocates, and others that reviews clinical trial protocols before they can be initiated. IRBs ensure that the trial is scientifically sound, ethical, and that the rights and safety of participants are adequately protected.

K

Key populations: groups of people such as sex workers, people who use drugs, prisoners, transgender people, and men who have sex with men that are at higher risk of HIV or TB, in part due to discrimination and social exclusion.

L

Latent TB infection (LTBI): a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens without evidence of active TB.

Live-vector vaccine: a vaccine in which a live pathogen is weakened (attenuated) through chemical or physical processes to produce an immune response without causing the severe effects of the disease.

Lymphadenopathy: enlargement of the lymph nodes in response to regional infection or inflammation.

Lymphocyte: a type of white blood cell primarily responsible for immune responses. Present in the blood, lymph, and lymphoid tissues. See also B cell and T cell.

Lymphoid tissue: the part of the body that plays an important role in the immune response and helps protect it from infection and pathogens. Lymphoid tissue is present throughout the body and includes the lymph nodes, spleen, tonsils, adenoids, and other organs.

Lymphomas: types of cancer that begin in the lymphatic system.

M

Macrophage: a large cell of the immune system that can ingest pathogens. Macrophages stimulate other immune cells by presenting them with small pieces of the pathogen. Macrophages also can harbour large quantities of HIV without being killed, acting as reservoirs of the virus.

Memory cell: a subset of T cells and B cells that help the body defend itself against disease by remembering prior exposure to specific pathogens. They can proliferate (recognise the antigen and divide) more readily when the immune system re-encounters the same pathogen.

Monoclonal antibody: a custom-made, identical antibody that recognises only one epitope.

Monocyte: a type of immune cell that is made in the bone marrow and travels through the blood to tissues in the body where it becomes a macrophage or a dendritic cell.

Monovalent vaccine: a vaccine that contains only one antigen.

Mucosal immunity: immune response pertaining to mucous membranes. Mucosal immunity relies on immune cells and antibodies present in the linings of the reproductive tract, gastrointestinal tract, and other moist surfaces of the body exposed to the outside world.

N

Natural killer cell (NK cell): a type of immune cell that can kill tumour cells or cells infected with a virus or bacteria. An NK cell is a type of white blood cell. NK cells are 'natural' killers because they do not need to recognise a specific antigen to attack and kill their target.

Neutralising antibody: an antibody that prevents a virus from infecting a cell in the body, usually by blocking receptors on the cell or the virus itself.

Nosocomial: an infection acquired or occurring in a hospital.

Nucleic acid: an important class of macromolecules found in all cells and viruses. Nucleic acids play an important role in how genetic information is stored and used.

Nucleic acid test (NAT): a laboratory test to detect the genetic material of a microorganism. The viral load (HIV RNA) test is a type of nucleic acid test.

O

Off-label use: the legal use of a prescription drug to treat a disease or condition for which the drug has not already been approved by the regulatory authority.

Open-label trial: a type of clinical study in which both the researchers and the participants are aware of the drug or treatment being given.

Opportunistic infection: an illness caused by an organism that usually does not cause disease in a person with a healthy immune system.

P

Pandemic: An epidemic occurring over a very wide area (several countries or continents) and usually affecting a large proportion of the population.

Parenteral: administered into the bloodstream or by injection.

Pathogen: organisms (e.g., bacteria, viruses, parasites, and fungi) that cause disease in human beings.

Pathogenesis: the origin and development of a disease. More specifically, the way a microbe (bacteria, virus, etc.) causes a disease.

Peptide: a short compound formed by linking two or more amino acids. Peptides that contain many amino acids are called polypeptides or proteins.

Phase I clinical trial: The first step in testing a new vaccine in humans. A Phase I clinical trial tests the safety, side effects, best dose, and timing of a new vaccine.

Phase II clinical trial: These trials measure safety and immunogenicity in a larger group (50–3000) of participants. Here the goal is also to find the best dose and regimen. Phase II trials may last up to two years or longer.

Phase III vaccine trial: A large study that tests the safety and how well a new vaccine works compared with a standard treatment.

Placebo: An inactive substance or other intervention that looks the same as, and is given the same way as, the vaccine being tested.

Plasma: The clear, yellowish, fluid part of the blood that carries the blood cells.

Preclinical: research often using animals to find out if a drug, procedure, or treatment is likely to be useful. Preclinical studies take place before any testing in humans is done.

Prevalence: the total number of individuals in a population who have a disease or health condition at a specific point in time, usually expressed as a percentage of the population.

Prime-boost: in HIV vaccine research, administration of one type of vaccine, such as a live-vector vaccine, followed by or together with a second type of vaccine, such as a recombinant subunit vaccine. The intent of this combination regimen is to induce different types of immune responses and enhance the overall immune response, a result that may not occur if only one type of vaccine were to be given for all doses.

Priming: the first dose of a vaccine given to induce a particular immune response, followed by or together with a second dose of vaccine. The intent of priming is to induce certain immune responses that will be enhanced by the booster dose(s).

Prophylaxis: the prevention of disease.

Protocol: the detailed plan for a clinical trial that states the trial's rationale, purpose, vaccine dosage, routes of administration, length of study, eligibility criteria and other aspects of trial design.

R

Randomised trial: a study in which participants are assigned by chance to one of two or more intervention arms or regimens. Randomisation minimises the differences among groups by equally distributing people with particular characteristics among all the trial arms.

Reactogenicity: physical reactions that occur soon after vaccination and are a physical manifestation of the inflammatory response to vaccination.

Reagent: any chemical used in a laboratory test or experiment.

Receptor: a molecule on the surface of a cell that can recognise and bind to other molecules such as antigens, antibodies.

Recombinant DNA technology: the technique by which genetic material from one organism is inserted into a cell to mass produce proteins.

Regulatory gene: genes that regulate the replication of pathogens.

Reservoir: HIV-infected cells that are not actively producing HIV.

Retrovirus: viruses that carry their genetic material in the form of RNA rather than DNA and have the enzyme reverse transcriptase that can transcribe it into DNA. In turn, this DNA will be used to create viral RNA in the infected cells.

Reverse transcriptase: the enzyme found in retroviruses that enables them to direct a cell to make DNA from their viral RNA.

RNA (ribonucleic acid): one of two types of nucleic acid made by cells. RNA contains information that has been copied from DNA (the other type of nucleic acid). Many forms of RNA have functions related to making proteins.

S

Seroconversion: the production of antibodies against a particular antigen in the blood of a person who did not have the antibodies before. When people develop antibodies, they 'seroconvert' from antibody-negative to antibody-positive (see also VISP).

Serostatus: the state of either having or not having detectable antibodies against a specific antigen, as measured by a blood test (serologic test).

Serum: the clear, yellowish liquid part of blood that remains after clotting. Serum is used for various laboratory tests.

Simian-Human Immunodeficiency Virus (SHIV): a genetically engineered hybrid virus with a human virus envelope and a simian virus core.

Side effect: see adverse reaction.

Simian Immunodeficiency Virus (SIV): a diverse group of viruses that naturally infect a wide range of African monkeys. This infection generally does not result in immunodeficiency in African monkeys, but Asian or Indian rhesus macaques will develop simian AIDS (SAIDS).

Statistical significance: a mathematical measure of difference between groups in a clinical study. The difference is said to be statistically significant if it is greater than what might be expected to happen by chance alone.

Sterilising immunity: an immune response that completely prevents the establishment of an infection.

Strain: a specific version of virus of bacteria. Many diseases, including HIV and Lassa fever virus have multiple strains.

S

Stratification: separation of a study cohort into subgroups or strata according to specific characteristics.

Subtype: a subgroup of genetically related HIV-1 viruses. Also called a clade.

Subunit vaccine: a vaccine that contains only part of the virus or other pathogen which have been specially selected for their ability to stimulate immune cells.

Surrogate marker: substitute measure of a clinical or biological endpoint. For example, CD4 count is a surrogate marker of disease progression.

T

T cell: a type of white blood cell critical to the immune response. Among these are CD4 T cells and CD8 T cells.

Therapeutic HIV vaccine: a vaccine designed to boost the immune response against HIV in a person living with the virus to slow the progression of HIV infection or delay the onset of AIDS.

V

Vaccine: a substance administered to trigger an immune response against a particular disease to prevent an infection.

Vector: a bacteria or virus that does not cause disease in humans and is used in genetically engineered vaccines to transport genes coding for antigens into the body to induce an immune response.

Viral Load (VL): the amount of HIV in a sample of blood. Viral load is reported as the number of HIV RNA copies per millilitre of blood.

Viremia: the presence of virus in the bloodstream.

Virion: a mature infectious virus particle that exists outside of a cell.

Virus: a microorganism that infects cells and may cause disease. To reproduce, a virus must infect a cell and direct its cellular machinery to produce new viruses.

Vaccine-Induced HIV Seropositivity (VISP): antibody induced by vaccination and that can confound the interpretation of HIV diagnostics tests. VISP may have implications in the everyday life of clinical trial participants (for example access to insurance, employment, or immigration).

W

Western blot: a laboratory test to detect antibodies to specific components of a virus such as HIV in the blood.

Window period: the period of time from exposure to HIV to when the body produces enough HIV antibodies to be detected by standard HIV tests.

RESOURCES

- NIH glossary of HIV/AIDS-related terms: *https://clinicalinfo.hiv.gov/en/glossary*
- CDC Vaccines and immunisation glossary: *https://www.cdc.gov/vaccines/terms/glossary.html*

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