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.

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And many other generous individuals and partners around the world

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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

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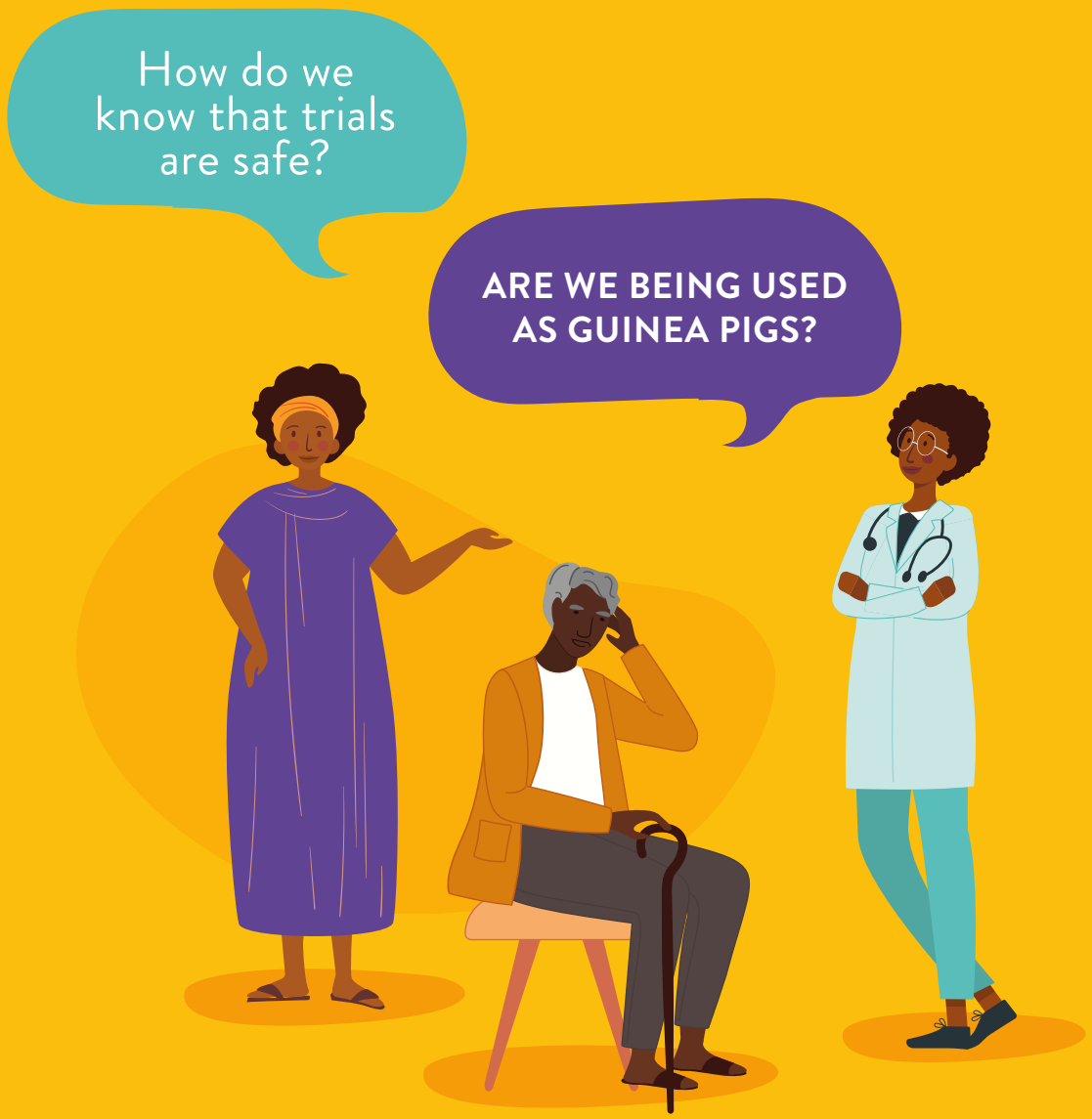
MODULE 6:
THE ETHICS AND REGULATION OF CLINICAL TRIALS



MODULE 6

THE ETHICS AND REGULATION OF CLINICAL TRIALS

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» Summary Points

- All clinical trials are carefully evaluated before they can start to make sure that they are scientifically and ethically sound, and most importantly, safe for participants.
- Independent review committees and regulatory authorities at local and international level conduct additional reviews as a trial is carried out to ensure they meet ethical standards and have the power to stop a trial at any time.
- All vaccine trials follow the same set of international ethical guidelines to ensure that each participant's health, dignity, and well-being are protected.
- Obtaining each participant's informed consent to participate in a trial is essential to ethical research; the purpose is to ensure that participants fully understand essential information about the trial and that they are not unfairly influenced to participate.

1. Introduction

All medical research is governed by principles of ethics. The same legal and ethical standards that are used for regular medical practice also apply to clinical trials, no matter in which country they are conducted. Additional consideration is given for the protection of clinical trial participants.

All vaccine trials follow the same set of international ethical guidelines to ensure that each participant's health, dignity, and well-being are protected. It is the duty of researchers to make sure that local standards of health and human rights of participants are also upheld.

Every clinical research project or study involving humans must go through a standard review process. This includes a review of both the product or vaccine to be tested, and the plan for how the study will be done, known as the protocol. The purpose of the review is to ensure first and foremost that the product is safe for testing in humans and that there are strong reasons for the specific study. Studies that do not enhance or advance our knowledge of human health would be considered unethical and not permitted.

2. Principles of Ethical Research

Researchers and ethical authorities work to ensure that research is conducted according to high ethical standards.

Seven primary principles form a basis for ethical conduct of clinical trials. These are principles for all types of clinical research and are applied to vaccine trials (see **BOX**).

The Seven Primary Principles of Ethical Research

1. **Value** – should answer a question that will enhance health or provide useful knowledge in the health field (see also **MODULE 1**).
2. **Validity** – should have an appropriate, careful, practical design and methodology (see also **MODULE 5**).
3. **Fair participant selection** – participants should be selected in a fair manner, based on scientifically and ethically sound factors (see also **MODULE 5** – Participation).
4. **Favourable risk/benefit ratio** – risks of participating should be kept to a minimum and should be justified by benefits of participating and of knowledge gained by the study.
5. **Independent review** – independent ethical and regulatory committees must review and give approval for the study.
6. **Informed consent** – every participant must understand the process, risks, and benefits of trial participation so she or he can make an educated and independent decision to participate.
7. **Respect for participants** – rights and welfare of participants must be protected throughout the entire trial, conclusion, and afterwards (follow-up).

2.1 Value

Every clinical trial or research study is designed to answer a specific question. Answering certain questions will have significant value for society or for people with a particular illness, now or in the future.

An answer to the research question should be important or valuable enough to justify asking people to accept some risk or inconvenience for others. Answers to the research question should contribute to scientific understanding of health or improve our ways of preventing, treating, or caring for people with a given disease or condition.

Clinical trials can only be justified if society will gain useful knowledge from the research.

MODULE 1 sets out the reasons why vaccine clinical trials for infectious diseases such as HIV, TB, and Lassa fever are vitally important.

2.2 Scientific Validity

Once it has been established that the clinical trial is answering a valuable research question, it should be designed in a way that will get an 'understandable answer.'

This includes considering whether the question researchers are asking is answerable, whether the research methods are valid and feasible, and whether the study is designed with a clear scientific objective and using accepted principles, methods, and reliable practices.

Invalid research is unethical because it is a waste of resources and exposes people to risk for no purpose.

See **MODULE 5** for a more detailed explanation of the methods and best practices that clinical trials use to ensure they deliver clear answers.

2.3 Fair Participant Selection

In order to answer the research question, scientists must consider who the study needs to include. The primary basis for recruiting and enrolling groups and individuals should be the scientific goals of the study — not vulnerability, privilege, or other factors unrelated to the purposes of the study.

Consistent with the scientific purpose, people should be chosen in a way that minimises risks and enhances benefits to individuals and society. Groups and individuals who accept the risks and burdens of research should be in a position to enjoy its benefits, and those who may benefit should share some of the risks and burdens.

Specific groups or individuals (for example, women or children) should not be excluded from the opportunity to participate in research without a good scientific reason or a particular susceptibility to risk.

This is further explored in **MODULE 5**.

2.4 Favourable Risk/Benefit Ratio

Participating in any clinical trial involves both risks and benefits. There will always be uncertainty about these, especially in the early trial stages. At the same time, participants may benefit from receiving health services that may not be otherwise available in that location, although the purpose of clinical trials is not to provide health services. These are important ethical considerations.

When researchers plan a study, they must make sure that the risks and benefits of participation have been thought through. If the relative balance of risks and benefits is not reasonable, the trial will not be seen as fair. If there are many risks, it is unfair to ask people to participate. On the other hand, if the standard of care within the trial is higher than outside the trial, people may participate for the wrong reasons and the study may be considered coercive.

When someone is deciding whether or not to participate in a trial, that person must fully understand the risks and benefits involved to make an informed choice of whether he or she feels that the benefits outweigh the risks of participation.

An ethical review board determines the balance of risks and benefits. Every study plan, or protocol, must be reviewed by such a board before the trial is approved.

Examples of Risks and Benefits in HIV Prevention Trials

Examples of risks include:

- Physical side effects of the candidate vaccine, such as a sore arm, headache or fever, and possible serious adverse events (SAEs).
- Social risks such as stigma or discrimination that may be associated with participating in a vaccine trial.
- False sense of protection from the vaccine, which may cause participants to be less careful about exposure to HIV, or risk behaviour.
- False-positive HIV antibody tests (in a person who received vaccine but does not have HIV); the risk of this happening and the time it might last are as yet unknown (see **BOX VISP**).
- Participants may not be able to donate blood during or after the trial, if they have antibodies that cause their blood to falsely test positive for HIV.

Benefits vary from place to place and person to person. Some potential benefits that have been cited include the following:

- Rewarding feeling of being involved in the clinical trial team — some participants report feeling that the staff becomes a 'family' or the study clinic, a place of comfort.
- Rewarding feeling of contributing to important medical research.
- Better understanding of HIV and how to avoid becoming infected.
- Receiving medical attention — although this must NOT be confused with standard health care, it may be attention an individual would not receive otherwise; for example, HIV counselling and testing, routine blood analysis/ monitoring.

Also known as vaccine-induced seropositivity (VISP)

False positive tests in HIV vaccine clinical trials

One of the potential risks of participating in a vaccine trial is testing 'antibody positive' for HIV, due to what is known as **vaccine-induced seropositivity (VISP)**. Many diagnostic tests use antibodies to diagnose infection, but they are unable to tell if those antibodies are from a vaccine or from natural exposure to disease.

For example, a participant in an HIV vaccine trial may falsely test HIV positive after the trial because of antibodies stimulated by the vaccine, even though the participant is not actually HIV positive.

This is particularly a risk for young people, as a false positive result may present potential barriers to pursuing college education, military service, seeking employment, getting married, and obtaining health insurance.

False positivity may or may not happen depending on the way the vaccine is designed, and if it does happen, it is not certain how long it will last. If this does happen, there are other tests that can easily be done to establish true infection (see **MODULE 3**) and the trial should provide documentation to enable the participant to explain false positivity, for example for insurance, travel, or blood donation purposes.

2.5 Independent Review

Before a trial can be conducted anywhere in the world, it must go through a scientific and ethics review.

All clinical trials are conducted according to a carefully controlled protocol, a detailed description, or guidelines, for how the trial will be carried out. All protocols must be carried out according to strict international standards, such as guidelines set by the International Council for Harmonisation (ICH) on Good Clinical Practices (GCP) and Good Clinical Laboratory Practices (GCLP).

Before any protocol can begin, it must be reviewed and approved by an ethics committee and relevant regulatory committees at the national level. Both national and international authorities that are independent of trial researchers and sponsors conduct ongoing monitoring of research projects to ensure that they meet ethical standards.

Review by Regulatory Authority

A National Regulatory Authority (NRA) generally reviews the information about the product (for example, the candidate drug or vaccine) as a whole, as well as the protocol that explains how a particular study of the product will be done. The NRA is ultimately responsible for approval of the specific study and approving and licensing the product for use in that country.

NRA approval is for clinical trials in the country itself, and if a study is done in more than one country, an NRA from each country must give approval. A report of the progress and results of the trial is sent regularly to the NRA.

Regulatory Authorities are not the same as Independent Ethics Committees, that focus solely on how the clinical trial is conducted.

Review by an Independent Ethics Review Committee

Before any candidate vaccine is tested in people, independent ethics committees (IECs), also called ethics review committees (ERCs) or institutional review boards (IRBs) from the institutions where the clinical trial will be conducted must review specific documents and approve the trial. This review process is designed to ensure the safety, human rights, and wellbeing of the participants involved in the trial.

The names of these review committees can differ from country to country (and even within the same country may differ from institution to institution), but they are all set up in a similar way and abide by the same set of principles.

After the IEC reviews the protocol and all trial-related documents (including recruitment advertisements and community education materials), they may make suggestions and recommend or require changes. The committee will document its recommendations to the site's Principal Investigator (PI), who will then communicate the recommendations or requirements to the sponsor. Trial sponsors and PIs may respond to concerns in writing. If required changes are made to the protocol or other documents, they need to be resubmitted for approval. A trial can begin only after all of the committees have given their final written and dated approval. More than one ethics committee may need to approve a protocol if different groups are involved.

After a vaccine trial begins, committees receive regular reports, including safety data summaries, notification of serious adverse events according to their requirements, and new information on the vaccine that allows them to monitor the safe and ethical conduct of the trial. In particular, committees make sure the investigator and sponsor are fulfilling their obligations to participants. These committees also have the power to stop the trial if there are any concerns for safety or if the trial is not being conducted ethically.

Local Ethics Committees

To ensure that trials are conducted according to ethical standards, a locally based ethics committee must review the proposed trial protocol, informed consent, and other study-related materials. The ethics committee may be called an ethics review committee (ERC) or an institutional review board (IRB). The main purpose of these committees is to ensure the safety and respect of human rights of trial participants and the ethical conduct of the trial.

These committees are made up of scientists, ethicists, community members, and other experts who are independent of the trial sponsors and investigators and are trained in evaluating research proposals. Ethics review committees should also include individuals with gender expertise to ensure that gender issues are considered during the review of the informed consent process and that decision-making is truly informed and voluntary.

This combination of people provides an unbiased, fair, and well-rounded evaluation of the study proposal. In addition to the ethics review, the ERC, IRB, or a related committee usually also conducts a science review.

Data and Safety Monitoring during Clinical Research

Participant's safety during clinical research is constantly monitored by internal and external monitoring boards.

Protocol Safety Review Teams (PSRTs)

The PSRT is an internal review committee that consists of the study principal investigators, and medical and other representatives of the study sponsor. The PSRT conducts day-to-day reviews (typically by conference call) of the safety data reports generated on a regular basis during the study. The PSRT also meet by conference call as needed to discuss any potential safety concerns. Not all studies include a PSRT.

Data Safety Monitoring Board

The Data Safety Monitoring Board (DSMB) or Independent Data Monitoring Committee (IDMC) is a multidisciplinary group of independent experts made of physicians from relevant medical specialties and biostatisticians. The DSMB may include other experts such as bioethicists, epidemiologists, and basic scientists. The DSMB conducts interim monitoring of the data from research activities as they arise to ensure the continuing safety of research participants, relevance of the study question, appropriateness of the study, and integrity of the accumulating data.

Community Advisory Boards (CABs)

Community Advisory Boards (CABs) are composed of leaders and other individuals representing various parts of the community, such as religious groups, schools or universities, media and non-governmental or community-based organisations, who review protocols and the informed consent documents, and help educate and inform the rest of the community.

Although CABs often provide feedback on research protocols, this is not considered official approval. Such groups often provide valuable insight that helps improve the trial process and are therefore important for a successful trial.

Often a senior scientist or medical professional and/or another member of the trial staff attends CAB meetings with some regularity, which is a sign of the CAB's significance in the trial process.

CAB members may take a very active role in planning for and undertaking vaccine trials. Some examples of their activities include the following:

- General community outreach and education.
- Support for participant recruitment by disseminating information about the trial.
- Providing feedback to the study team on trial protocols, including criteria for participation, informed consent forms and processes, and participant recruitment and retention.
- Keeping track of community views and concerns about the trial including rumours and misinformation related to the trial.
- Advising investigators regarding potential participants' perspectives about the trial.
- Providing a safeguard (in addition to institutional ethics review committee) for participants' rights.
- Representation at important national, regional, and international meetings and conferences.

Most researchers acknowledge that for a trial to be successful, it is important to obtain general support from the communities that will be involved in the research. As the CAB acts as a liaison between the researchers and the community, researchers may hold consultations with CABs about an upcoming trial.

2.6 Trial Guidelines

All review committees follow internationally agreed-upon guidelines that provide detailed definitions of the requirements for ethical research. These guidelines create uniform ethical and scientific standards for all trials with human participants, wherever they take place.

International Council for Harmonisation (ICH)

The International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) brings together regulatory authorities and the pharmaceutical industry to discuss scientific and technical aspects of pharmaceuticals and develop ICH guidelines. ICH's mission is to achieve greater harmonisation worldwide to ensure that safe, effective, and high-quality medicines are developed, registered, and maintained in the most resource efficient manner whilst meeting high standards.

Good Clinical Practice (GCP)

Good clinical practice is an international quality standard based on the ICH. The official guidelines for GCP were established by the U.S. Food and Drug Administration (FDA), in agreement with the ICH. The purpose of the guidelines is to establish standards for designing, conducting, recording, and reporting clinical trials. These guidelines establish the requirements needed for effective review and approval of proposed clinical studies.

Good Participatory Practice (GPP)

Good Participatory Practice (GPP) guidelines provide clinical trial funders, sponsors, and implementers with systematic guidance on how to effectively engage with all stakeholders in the design and conduct of vaccine biomedical research. Guidelines also exist for emerging infectious diseases.

Specific Guidance

HIV vaccine research involves unique additional ethical issues. The Joint United Nations Programme on HIV/AIDS (UNAIDS) has helped to address them by issuing an official ethics guidance document, found in the resources section below.

ETHICS AND SCIENTIFIC ADVISORY COMMITTEES

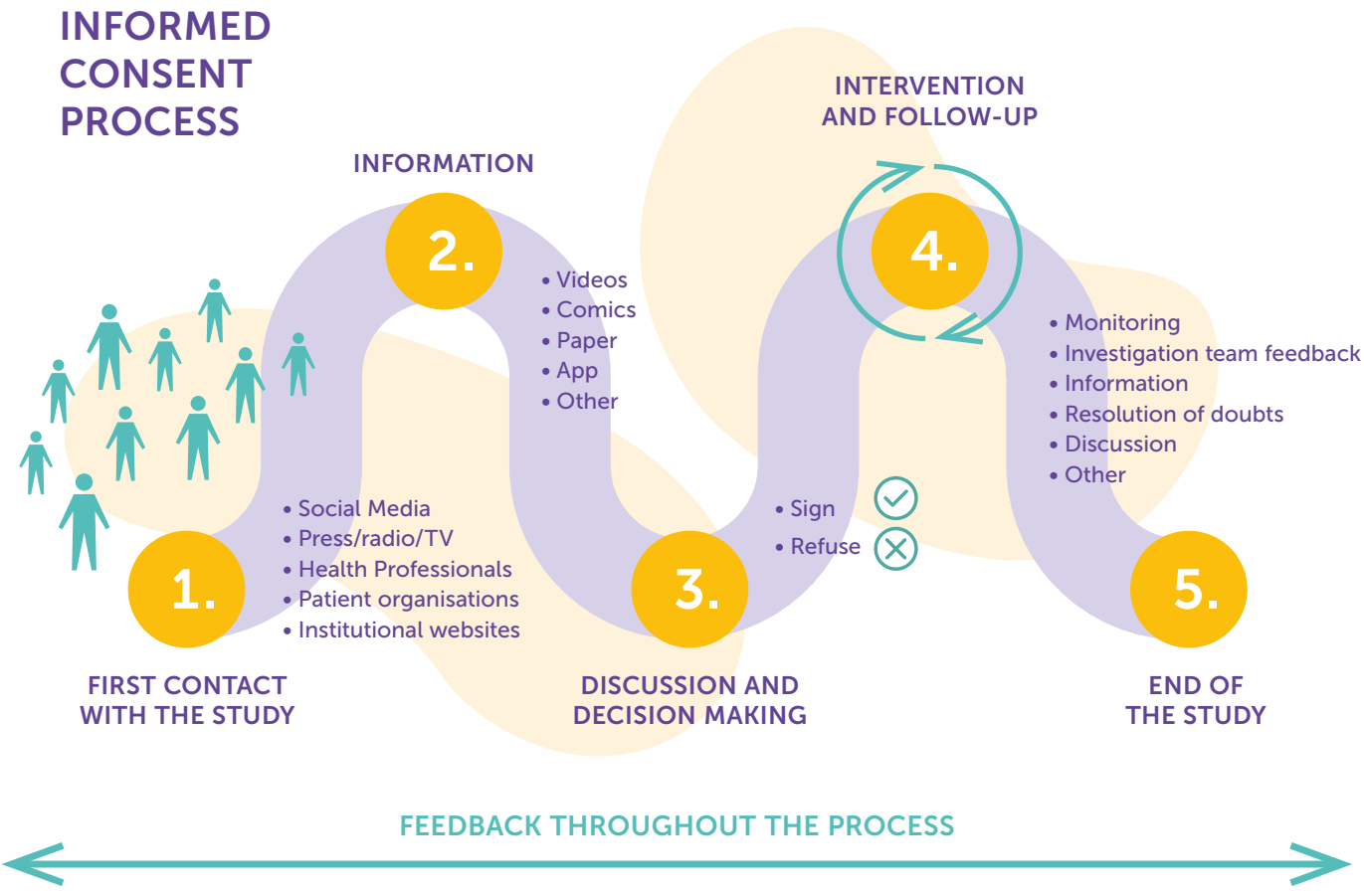
	REGULATORY	SCIENTIFIC	ETHICS
Focus of information reviewed	Package for review includes all relevant information about the product, including all previous tests (preclinical and clinical) done on the product and how it will be tested in humans, including protocol for testing the product, and the Investigator's Brochure.	Scientific committee review ensures that the trial is asking legitimate scientific questions and that the study is well designed to answer these questions. NOTE: Scientific review may be carried out by an ethics committee.	Package for review includes all relevant information about the protocol, focusing on one study of the product to be conducted at a specific institution. Some also include review of the product, usually based on the Investigator's Brochure.
Level of committee	Country/national, appointed by government; sometimes regional.	Institution/university or country/national.	Institution/university in most cases; national in some cases.
Materials reviewed	Product specific materials — entire package of information on preclinical and clinical testing of the product, its safety and its biological effects and rationale for specific details of testing; trial-specific materials (such as the protocol) are also reviewed.	Product- and trial-specific materials.	Trial-specific materials — study protocol, including the informed consent, advertisements for study recruitment, informed consent document.
Examples	U.S. Food and Drug Administration (FDA); National Council of Science and Technology of Government of Kenya.	Institutional Review Board (IRB) at an academic institution involved in the trial.	Kenyatta National Hospital Ethical and Research Committee — a joint committee between the University of Nairobi and Kenyatta National Hospital.

2.7 Informed Consent

Informed consent is not a one-off event but is 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 enrolled in 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.

Researchers cannot rely on this document alone to ensure that the individual truly understands the trial. Obtaining true informed consent involves a process of delivering information about the trial, making sure people understand the information and ensuring that the participant makes his or her own decision to participate. Community education is an important part of this process of education and dialogue between researchers, communities, and potential participants.

Obtaining true informed consent can be a challenge in communities that are not familiar with medical research or with vaccines, and in populations or individuals that may be vulnerable to pressures from others. This means that potential participants must fully understand key aspects of trial participation, including the potential risks and benefits (see below), before they sign the informed consent form. In many trial sites, this involves two levels of outreach, one to the broader community and one to the individual.



Although informed consent is not the only factor in ensuring the ethical conduct of a trial, it is a key factor. The researchers must explain to participants many important facts about the trial, including its purpose, the vaccine that will be tested, the number of clinical visits required, and possible benefits and risks. Participants also need to know that they have the right to not participate or to withdraw at any time. Importantly, researchers must be sure that the participant's decision is free from inducement or coercion of any kind. This should be clearly presented in the informed consent document (see **BOX**).

The Informed Consent Document

The informed consent is the document signed by anyone who decides to participant in a trial that indicates his or her understanding of, and agreement to, the following:

1. Why the research is being done.
2. What researchers want to accomplish and who is responsible for the trial.
3. What will be done during the trial and for how long.
4. What risks are involved.
5. What is expected of trial participants.
6. What, if any, benefits can be expected from the trial.
7. The system in place for care and support of participants.
8. What other interventions are available.
9. The participant's right to leave the trial at any time.

Informed Consent and Specific Populations

Communicating the complete information and ensuring understanding can be complex and difficult, particularly for vulnerable groups, as well as women and adolescents in specific situations.

As part of the process of ensuring informed consent, the community at large should be provided with information about the trial. This process helps to create an environment that will help enable women, adolescents, and other vulnerable people to participate in trials. Giving informed consent and participating, however, is ultimately the individual's decision.

Vulnerable Populations

Specific measures should be taken to support and protect people who are, or who may be, limited in their ability to participate voluntarily or provide informed consent. This can include prisoners, and those who have limited literacy or low levels of education.

It is also important to consider that the populations who are recruited to clinical trials may be stigmatised, discriminated against, and criminalised in the country in which the research is taking place, such as people living with HIV, men who have sex with men, transgender people, sex workers, and people who use drugs.

Information must be presented in language that all participants understand, in a way that prepares people to fully understand their rights, risks, and benefits and in an environment that supports independent decision-making. All participants should fully understand the information provided before they sign an informed consent form.

Women

In some contexts, women may be vulnerable to unfair influence and coercion from husbands, family, community members, and healthcare providers to sign consent forms. Many women may want to discuss potential participation with important people in their lives, including husbands, partners, and fathers. It is important for these women to have the opportunity to consult with whomever they wish, but they should know that this is not required for informed consent.

To participate in a trial, only the woman's personal, individual informed consent is required. As explained below, her confidentiality is always protected if she wants to participate but does not want to inform others, for example a male partner.

Adolescents

It is important to include young people in vaccine clinical research for a number of reasons.

The optimal age for vaccination may be before puberty, and data on how vaccines work in young people are usually required by regulatory authorities to be sure of safety. Young people, especially young women, are also among the highest risk group for several sexually transmitted infections, including HIV.

However, in most countries, young people under the age of 18 are legal 'minors' and therefore usually unable to give consent for participation in clinical research without parental permission. Parents may be reluctant to give consent due to stigma, and young people may be unwilling to ask. Patient confidentiality about sexual history and reproductive health may conflict with the local expectations around the age of consent. Adolescents may not fully understand their personal risk, posing challenges for informed consent as well as prevention counselling during the trial.

It is vitally important that additional regulatory and ethical safeguards are put in place to protect adolescents, but equally vaccine trial sites need to be youth-friendly and cater specifically to their unique needs.

2.8 Respect for Participants

Protection of trial participants is a human rights issue and has become a defining factor in the conduct of all vaccine trials.

Participants do a service for researchers and for medical science in general and it is the duty of researchers to make sure participants are taken care of. Participating in a trial involves certain risks that a person may not encounter in normal daily life, as discussed above. Individuals should be treated with respect from the time they are approached for possible participation — even if they refuse enrolment in a study — throughout their participation and after their participation ends. This includes informing participants and the community about what was learned from the research by sharing the results.

Welfare

Researchers should take measures to protect the safety, human rights and welfare of participants, and to prevent discrimination or prejudice. For example, they may take professional development courses on stigma in health care and other settings, or on culturally appropriate care and language. Staff in the trial sites should be educated about stigma and discrimination around key populations, gender, human rights and health care, and gender-based violence. Staff should know how to identify participants affected by these issues and be familiar with the resources available or services to refer them to.

When monitoring participants' welfare, the study team must be able to ensure appropriate treatment and support if they experience adverse reactions or change in clinical status. Participants must be informed of any new information that emerges, which might change their assessment of the risks and benefits of participating. Researchers must respect their right to change their mind, to decide that the research does not match their interests, and to withdraw without penalty.

Confidentiality

The study team must keep all information about participants confidential. Information collected about the participant during the trial should not be disclosed to anyone except study staff without the consent of the participant.

If a participant sees a doctor who is not involved in the trial for a medical problem, it is helpful to let the doctor know that he or she is participating in the trial, so the doctor can do a better job of treating the individual. However, the participant must provide that information themselves; the study team will not give the doctor information unless requested by the participant.

While confidentiality is critical for all trial participants, women may be particularly vulnerable if confidentiality is broken, as disclosure of participation in trials itself may lead to stigma, discrimination, and violence. This is particularly relevant to HIV vaccine trials: If a woman is known to be participating in such a trial, people may assume she is engaging in risky behaviour or that she is protecting herself from the risky behaviour of her partner. Similarly, there is considerable potential for stigma and discrimination against vulnerable and other marginalised populations. All trial staff must be trained in handling confidentiality in a diversity- and gender-sensitive manner.

3. Community Outreach

Outreach to the broader community extends beyond the scope of trial recruitment. It involves informing the leaders in a community well in advance of the trial as an important channel for building understanding and support among the community at large. Having leaders who are informed and supportive of the trial will also minimise stigma that may be attached to community members who participate or who even ask for information about the trial.

Most vaccine trial sites have active community advisory boards (CABs) that are an important form of outreach to the broader community, although alternative community advisory mechanisms may also exist. These groups act as liaisons between the trial researchers and the community, and they help to tailor and deliver the proper information to potential participants.

For outreach to the individual, a trial site will sometimes offer general information sessions, where anyone interested can learn about vaccine research. There may also be one-on-one counselling sessions where potential participants learn about the trial in more detail. Finally, some studies require that before signing the informed consent, potential participants complete a questionnaire to test comprehension.

FIND OUT MORE...

- International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. Copyright ICH Secretariat, Geneva, Switzerland. Online version: *https://www.ich.org*
- Good Participatory Practice Guidelines 2nd edition (June 2011): *https://www.avac.org/resource/good-participatory-practice-guidelines-biomedical-hiv-prevention-trials-second-edition*
- Science, theory, and practice of engaged research: Good Participatory Practice and beyond JIAS, (2018): *https://www.avac.org/sites/default/files/resource-files/JIAS_Vol21-S7.pdf*
- Good Participatory Practice for TB vaccine research: *https://www.avac.org/resource/good-participatory-practice-guidelines-tb-vaccine-research-2017*
- Ethical considerations in HIV prevention trials: *https://www.unaids.org/sites/default/files/media_asset/ethical-considerations-hiv-prevention-trials_en.pdf*
- WMA Declaration of Helsinki – ethical principles for medical research involving human subjects: *https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/*
- Research Fairness Initiative: *https://rfi.cohred.org*
- TRUST Equitable Research Partnerships*: http://trust-project.eu*

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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