

Building Resilience Against Outbreaks & Pandemics

Research to identify
sustainable solutions

The 3rd Global Research and Innovation
Forum



World Health
Organization



R&DBlueprint
Powering research
to prevent epidemics

Building Resilience Against Outbreaks & Pandemics

Epidemics, pandemics
and how research can
help to control them

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The Constitution of WHO states that one of WHO's key roles is to promote, conduct, and coordinate research in the field of health.

In May 2015, the 68th World Health Assembly welcomed the development of an R&D Blueprint for Epidemics, in consultation with Member States and relevant stakeholders, for accelerating research and development (R&D) in epidemics or health emergency situations where there are no, or insufficient, preventive and therapeutic medical countermeasures.



The research continuum – critical work delivered before, during and after outbreaks

**We cannot
make the world
safer without
investments
in science,
research and
innovation.**



Tedros Adhanom
Director-General
World Health Organization

Today, we stand at a crossroads in **shaping global resilience**, preparedness, and response strategies for the next major epidemic or pandemic.

It is critical that we assimilate the lessons learned from the pandemic and **harness the wealth of research knowledge, platforms and collaborative frameworks** forged during the COVID-19 crisis to help protect the world from future threats.

Coordinating and accelerating global research must promote universal values

Regarding a collaborative effort to ensure access to MCMs, some have emphasized the importance of **speed** and sometimes **cost** in responding to future pandemics.

It is equally important to take a broader view that recognizes the primary importance of **quality, equity** in availability, and **trust** in the products safety and efficacy.

Sometimes dreams become reality...

News of Ebola vaccine reaches
a rural village in Liberia in 2015

Local photographer Alphonso Appleton [#thankyouscience](#)



In 2014-16, an unprecedented and collaborative WHO-led effort built on a number of candidate Ebola vaccines that could enter clinical trials

A series of international consultations and activities were led by WHO as a contribution to the unprecedented global efforts to develop and assess an Ebola vaccine.



Panel discussion on ethical considerations for use of unregistered interventions for Ebola virus disease

Summary of the panel discussion

8 August 2014 | Departmental news (Reading time: less than a minute (2/7 words))

The recent treatment of two health workers infected with the Ebola virus with experimental medicine has raised questions about whether medicine that has never been tested and shown to be safe in people should be used in the outbreak, and, given the extremely limited amount of medicine available, if it is used, who should receive it.

A number of interventions have been through the laboratory and animal study phases of development. It is likely that first-in-man studies will be conducted over the next 2-4 months. It is also likely that the number of doses available for further study and/or deployment from end 2014 onwards will remain insufficient to meet demand.

On Monday, August 11, WHO is convening a panel discussion of medical ethicists, scientific experts and lay people from affected countries to assess the role of experimental therapies in the Ebola outbreak response.

Issues to be considered include:

- Whether it is ethical to use unregistered interventions with unknown adverse effects for possible treatment or prophylaxis. If it is, what criteria and conditions need to be satisfied before they can be used?

Ebola Vaccine — An Urgent International Priority

Rupa Karapathipalli, M.D., Ana Maria Henao Restrepo, M.D., Patricia Fast, M.D., Ph.D., David Wood, Ph.D., Christopher Dye, D.Phil., Marie-Paule Kieny, Ph.D., and Vasek Moody, B.M., B.Sc., Ph.D.

With the Ebola epidemic in West Africa continuing to grow, the World Health Organization (WHO) convened an urgent meeting on September 29 and 30 to assess the efforts under way to evaluate and produce safe and effective Ebola vaccines as soon as possible.¹ The 70 scientists, public health officials, and representatives from industry and regulatory bodies who gathered in Geneva discussed two vaccine candidates at length — cAd3-EBOV (cAd3, from GlaxoSmithKline (GSK)) and the U.S. National Institute of Allergy and Infectious Diseases (NIAID) and FVING-EBOV-GP (FVING), from Novartis Genentech and the Public Health Agency of Canada. Several other vaccine candidates are at earlier, preclinical stages in the development pipeline.

Phase 1 studies of cAd3 have begun in the United States and the United Kingdom, and researchers plan to begin enrollment for trials of FVING soon. Both vaccine candidates have demonstrated 100% efficacy in studies in nonhuman primates,^{2,3} but how that will translate to human subjects remains unknown. The phase 1 trials of both vaccines use dose-response designs structured to determine the level of humoral and cellular immunity that can be induced. The minimum antibody titer needed to confer protection in humans is unknown. Because of the small numbers of participants in these trials, they will provide data only on common adverse events.

The cAd3 vaccine is being tested in both bivalent (ClinicalTrials.gov number: NCT02111846) and monovalent (NCT02040875) forms; the monovalent form is based on the Zaire strain of Ebola virus, which is the cause of the current West African epidemic, and the bivalent form includes the Sudan strain of the virus as well (see Fig. 1). The monovalent form will be evaluated in a nonrandomized, open-label study involving 60 adult volunteers who will receive the vaccine at three different doses (1x10⁸ vp, 2.5x10⁸ vp, and 5x10⁸ vp). The bivalent form will be evaluated in a nonrandomized, open-label study involving 20 adult volunteers who will receive the vaccine at two different doses (2x10⁸ vp and 2x10⁹ vp). Both studies will assess safety, side effects, and immunogenicity, including antibody responses as measured by enzyme-linked immunosorbent assay (ELISA) and neutralization assays and T-cell immune responses as measured by intracellular cytokine staining. Investigators anticipate that preliminary immunogenicity and safety data will be available by November.

Emergency use listing procedure

Version 8 August 2014

1 January 2014 Publication

Overview

The World Health Organization (WHO) developed the Emergency Use Assessment and Listing (EUAL) mechanism in response to the 2014–2016 Ebola Virus Disease (EVD) outbreak. The EUAL is a risk-based procedure for assessing and listing unlicensed vaccines, therapeutics and in vitro diagnostics (IVDs) for use primarily during public health emergencies of international concern (PHEIC) but also in other public health emergencies if appropriate.

Two submissions for Ebola vaccines were received but none was listed. No therapeutic products that were in development were submitted during the 2014–2016 Ebola outbreak. Twenty-five applications for IVDs were received for Ebola assays of which seven were listed. Also, three out of thirty-three applications received for IVDs were listed.

Based on the above experience, vaccine developers and national regulators identified the need to revise and simplify the procedure, in order to improve clarity on procedural aspects, and to avoid overlap or gaps in their respective functions.

WHO consulted widely and immediately fostered interactions

With the international scientific, ethics, regulatory, vaccine development, public health partners, industry, and funders' communities. WHO participated in consortia to facilitate Ebola vaccine assessments. WHO also fostered key activities to ensure the optimal policy and development of Ebola vaccines.

WHO High-level meeting on Ebola vaccines access and financing

23 October 2014

SUMMARY REPORT

World Health Organization

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Financing of R&D Preparedness and Response to Epidemic Emergencies

28–30 October 2015 | Oslo, Norway

The Oslo consultation is part of a response to the resolution made by WHO Member States in May 2015 (WHA68.10) which welcomed 'the development of a blueprint, in consultation with Member States and relevant stakeholders, for accelerating research and development in epidemics or health emergency situations where there are no, or insufficient, preventive, and curative solutions, taking into account other relevant work streams within WHO'. The Blueprint that is currently being developed by WHO consists of the main work streams:

- Prioritization of 5–10 pathogens and operational plan to transition from preparedness to response (Work stream 1)
- Identification of research priorities for the above priority pathogens (Work stream 2)
- Coordination of stakeholders and expansion of capacity (Work stream 3)
- Assessment of preparedness and impact of intervention (Work stream 4) and, finally,
- Exploration of funding models for R&D preparedness and response (Work stream 5).

The Oslo consultation focused on Work stream 5 and on how to ensure adequate and sustainable funding for R&D (preparedness and (ii) response to public health emergencies due to infectious diseases with epidemic or pandemic potential. Participants explored different options that would ensure that the required research

Phase 1 Trials of rVSV Ebola Vaccine in Africa and Europe

S.T. Agnandji, A. Huttmner, M.E. Zinszer, P. Njuguna, C. Djalile, J.F. Fernandes, S. Yerly, J.-A. Dayer, V. Kraehling, R. Kasonta, A.A. Adegnika, M. Alkfeld, F. Auderset, E.B. Bache, N. Biedenkopf, S. Borregaard, J.S. Broznan, R. Burrow, C. Camberiscura, J. Desmoules, M. Eichmann, S.K. Fehling, A. Finckh, A.R. Gonçalves, M.P. Grollman, J. Hooper, A. Jamboana, A.L. Kallensette, G. Kays, D. Kimani, B. Lali, B. Lemaitre, A.W. Lohse, M. Massing-Lambert, A. Mathay, B. Mondoulet, A. Naling, C. Ogoang, M. Ramtstein, J. Schmidt-Chanest, S. Schmiedel, P. Silvers, F.R. Stahl, H.M. Staines, T. Strecker, H.C. Stubbe, B. Tsolia, S. Zaki, P. Fast, V. Moorfly, L. Kaiser, S. Kishna, S. Becker, M.-P. Kiery, P. Bejon, P.G. Kremsner, M.M. Adda, and C.-A. Siegrist*

ABSTRACT

BACKGROUND
The replication-competent recombinant vesicular stomatitis virus (rVSV)-based vaccine expressing a Zaire ebolavirus (ZEBV) glycoprotein was selected for rapid safety and immunogenicity testing before its use in West Africa.

METHODS
We performed three open-label, dose-escalation phase 1 trials and one randomized, double-blind, controlled phase 1 trial to assess the safety, side-effect profile, and immunogenicity of rVSV-ZEBV in various doses in 158 healthy adults in Europe and Africa. All participants were injected with doses of vaccine ranging from 300,000 to 90 million plaque-forming units (PFU) or placebo.

RESULTS
No serious vaccine-related adverse events were reported. Mild-to-moderate early-onset reactogenicity was frequent but transient (median, 1 day). Fever was observed in up to 30% of vaccinees. Vaccine viraemia was detected within 1 days in 123 of the 130 participants (95%) receiving 3 million PFU or more; rVSV was not detected in saliva or serum. In the second week after injection, arthritis affecting one to four joints developed in 11 of 51 participants (22%) in Geneva, with pain lasting a median of 8 days (interquartile range, 4 to 8). 2 self-limited cases occurred in 60 participants (1%) in Hamburg, Germany, and Kilifi, Kenya. The virus was identified in one synovial fluid

Gavi commits to purchasing Ebola vaccine for affected countries

Vaccine Alliance ready to begin procurement as soon as WHO recommends a vaccine for use

Geneva, 11 December 2014. Plans to purchase millions of doses of an Ebola vaccine to support large-scale vaccination efforts were today agreed by the board of Gavi, the Vaccine Alliance. Today's decision means that Gavi will be ready to act as soon as a safe, effective vaccine is recommended for use by the World Health Organization.

RELATED DOWNLOADS

- Frequently asked questions about Gavi's plans to support a future Ebola vaccine



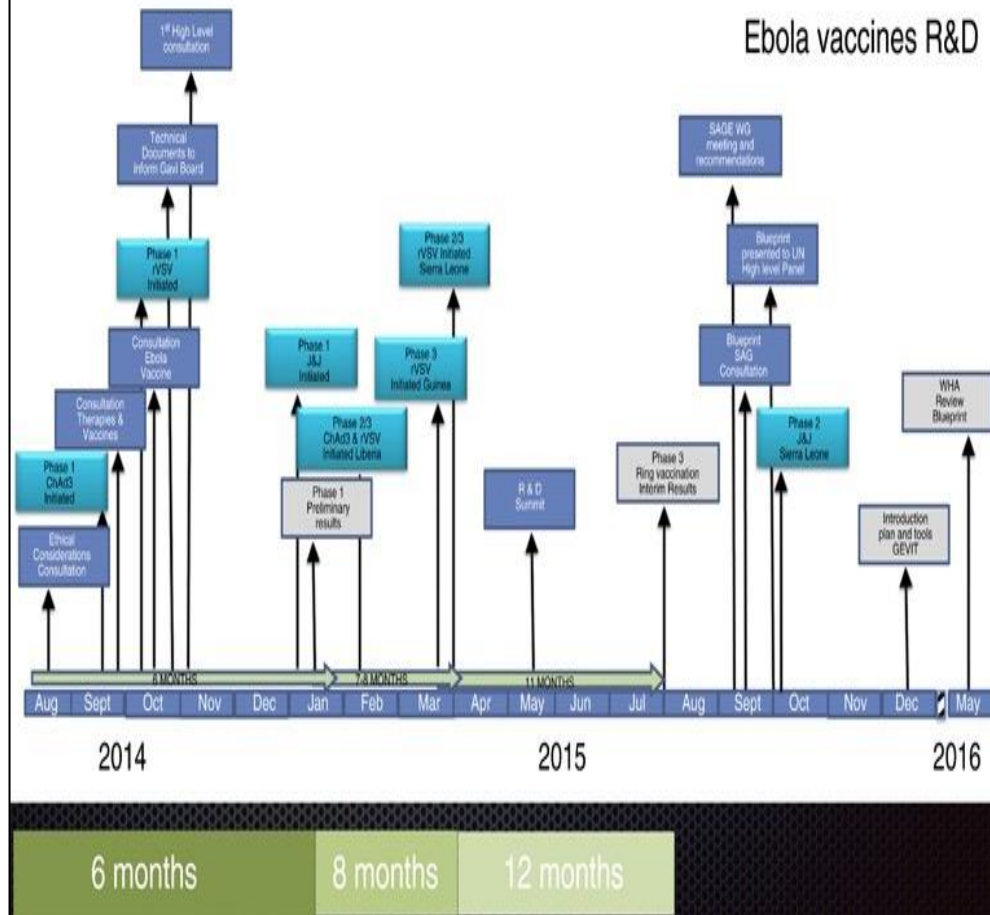


On a path to accelerate access to Ebola vaccines: The WHO's research and development efforts during the 2014–2016 Ebola epidemic in West Africa

Ana Maria Henao-Restrepo¹, Marie-Pierre Preziosi¹, David Wood²,

Vasee Moorthy¹, Marie Paule Kieny³ ✉,

the WHO Ebola Research, Development Team



A novel trial design with the country in the driving seat and 26 global institutions collaborating

Efficacy and effectiveness of an rVSV-vectored vaccine expressing Ebola surface glycoprotein: interim results from the Guinea ring vaccination cluster-randomised trial

Ana Maria Henao-Restrepo, Ina M Longini, Matthias Egger, Natalie F Dean, W John Edmunds, Anton Camacho, Miles W Carroll, Moussa Dombia, Bertrand Droguez, Sophie Duraffour, Godwin Enwere, Rebecca Grais, Stephan Gunther, Stefanie Hossmann, Mandy Kader Kondé, Souleymane Kane, Evee Kuluma, Myron M Levine, Sema Mandal, Gunstein Norheim, Ximena Riveros, Aboubacar Soumah, Sam Telle, Andres S Vicari, Conall H Watson, Sokobe Kliba, Marie Paule Kiery*, John-Arne Rattinger*

Summary

Background A recombinant, replication-competent vesicular stomatitis virus-based vaccine expressing a surface glycoprotein of Zaire Ebolavirus (rVSV-ZEBOV) is a promising Ebola vaccine candidate. We report the results of an



Lancet 2015; 386: 857-66

Published Online

July 31, 2015

[http://dx.doi.org/10.1016/S0140-6736\(15\)00107-6](http://dx.doi.org/10.1016/S0140-6736(15)00107-6)

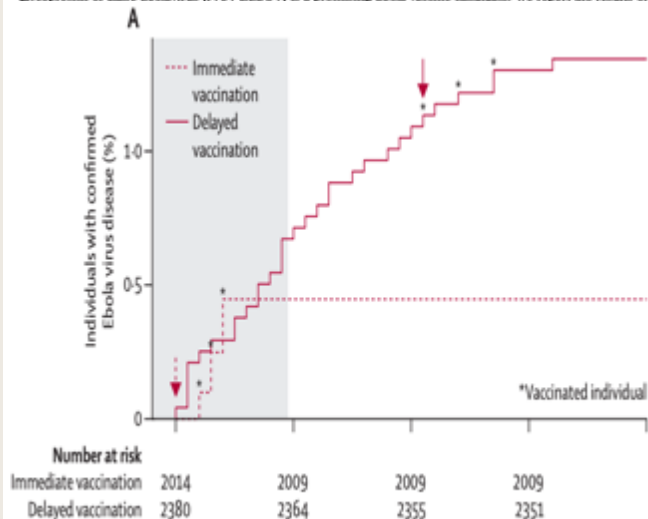
See Editorial page 833

See Comment page 833

*These authors contributed equally

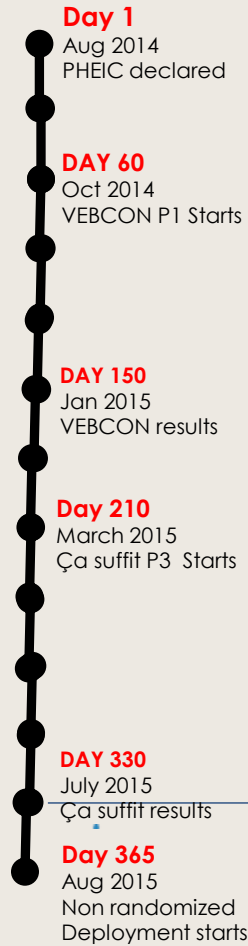
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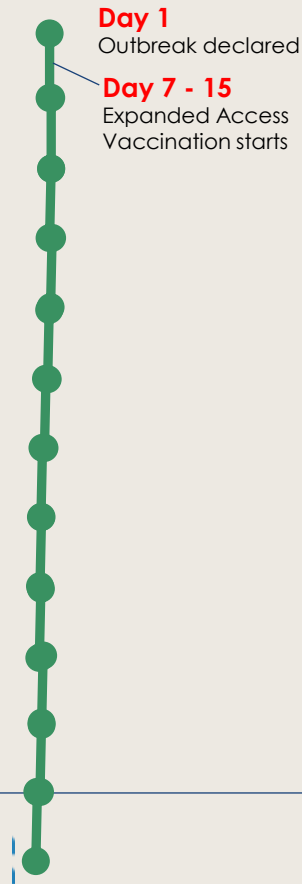


“The Dream Team”

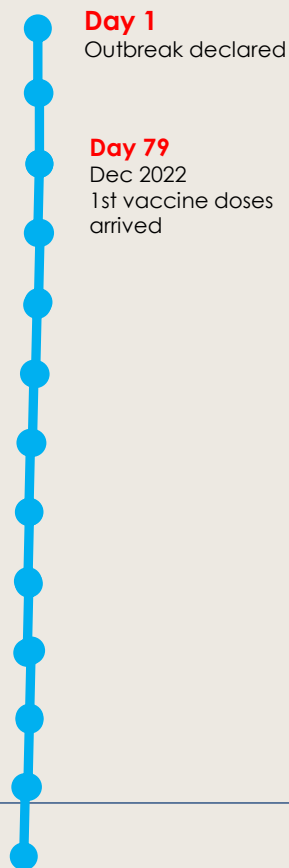
ZEBOV- RCT
VEBCON & Ça Suffit
Guinea 2014-2016



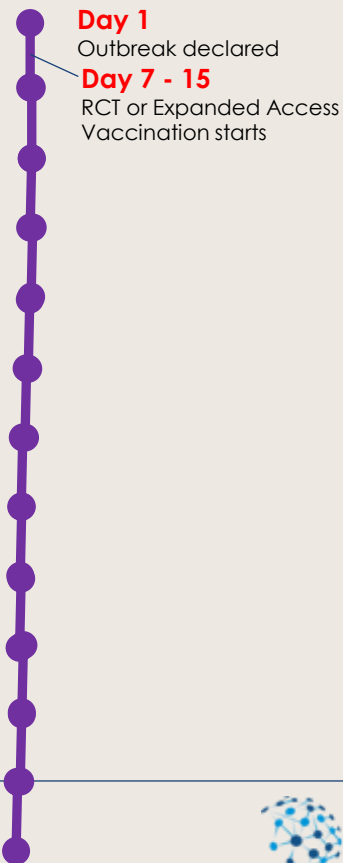
ZEBOV - Expanded Access
Guinea, Sierra Leone, DRC
2016 - 2020



SUDV - RCT
Uganda
2022



AIM
RCT or Expanded Access
NEXT OUTBREAK



Since 2016 all STUDIES STARTED PROMPTLY

- ✓ Previously agreed prioritization of candidate vaccines
- ✓ Phase1 (and 2 data)
- ✓ Funded investigational vaccines already in vials (internationally transferable)
- ✓ Previously established trial platforms
- ✓ Previously agreed simple protocol

Previously agreed:

- ✓ LEGAL collaboration,
- ✓ Insurance and
- ✓ Liability frameworks
- ✓ Previously agreed funding



R&DBlueprint
Powering research
to prevent epidemics

Expanded Access with rVSV ZEBOV GP

(unlicensed doses), for outbreaks reported between 2016 - 2022

12

12 EVD (Zaire) outbreaks and **3,721** EVD confirmed cases reported

Over **350,000 people at risk vaccinated**
(contacts and contacts of contacts) including **>100,000** HCWs/FLWs

Informed consent for all and individual data collection from 250,000



A COORDINATED GLOBAL RESEARCH ROADMAP: 2019 NOVEL CORONAVIRUS

MARCH 2020

There is broad consensus on the need for research to: focus on actions that can save lives now; facilitate actions so that those affected are promptly diagnosed and receive optimal care; and catalyse the full integration of all innovations within each research area.

Moreover, there is an imperative to support research priorities in a way that leads to the development of sustainable global research platforms pre-prepared for the next disease X epidemic. This will allow for accelerated research, innovative solutions and R&D of diagnostics, therapeutics and vaccines, as well as the timely and equitable access to these life-saving tools for those at highest risk.



COVID-19 Research and Innovation

Powering the world's pandemic response – now and in the future

February 2022



Global Research and Innovation for Health Emergencies

Building the world's resilience against
future outbreaks and pandemics

October 2023



R&DBlueprint
Powering research
to prevent epidemics

New strategic components steering future global research agenda

14



Countries begin negotiations on global agreement to protect world from future pandemic emergencies

3 March 2023 | News release | Geneva | Reading time: 2 min (464 words)

Media Contacts



WHO to identify pathogens that could cause future outbreaks and pandemics

21 November 2022 | News release | Geneva | Reading time: 1 min (388 words)

Media Contacts

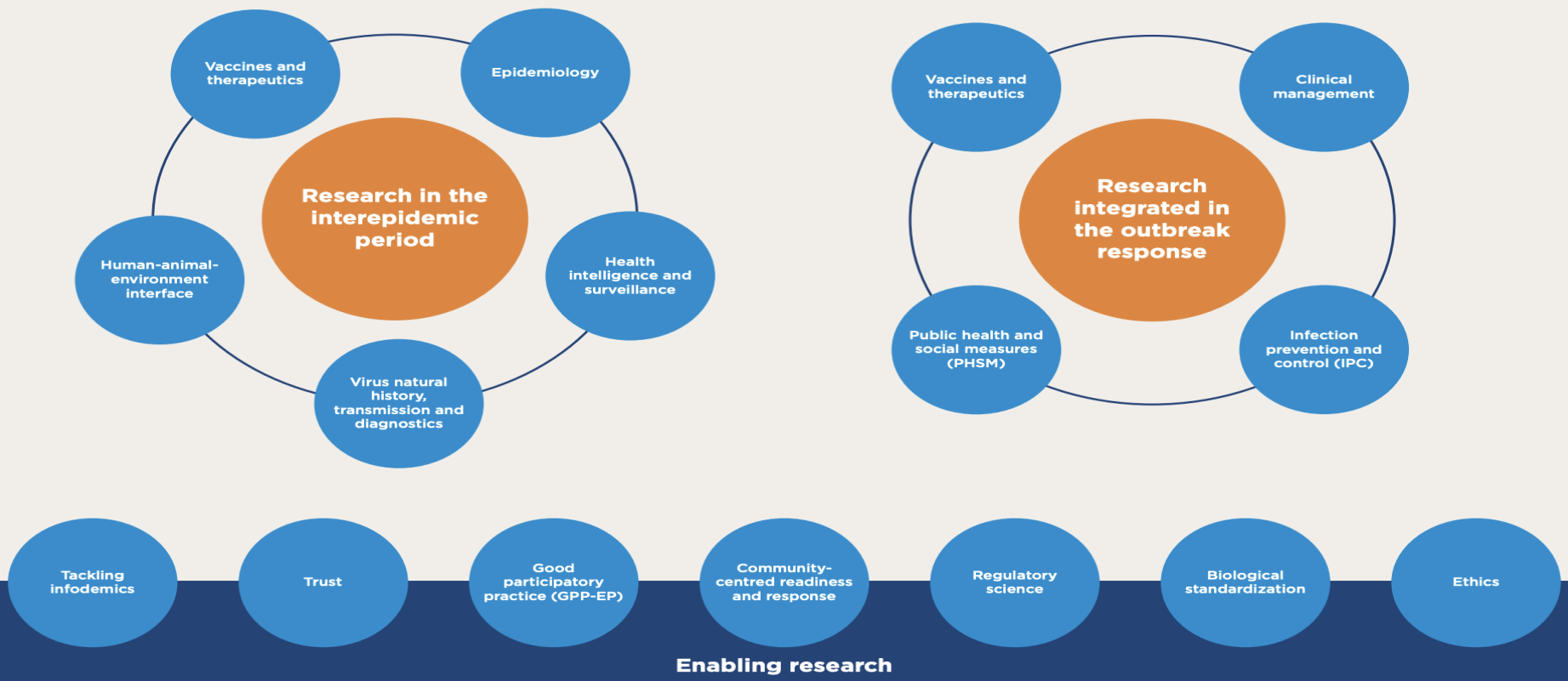
Core activities of the WHO R&D Blueprint for Epidemics toward a robust and coordinated global research response to emerging disease threats¹⁵

- Viral and Bacterial families prioritization
- R&D Roadmaps and Target Product Profiles (TPPs) for each prioritized viral and bacterial family
- Pipeline monitoring and prioritization for evaluation.
- Research in the context of outbreaks and pandemics
- Promotion of building capacities to conduct clinical trials and research in accordance with international standards.

Figure 1 shows progress on the delivery of key activities within the R&D Blueprint up to May 2023

Pathogen	RAD Roadmap	Vaccines					Therapeutics					Diagnostics					Research priorities for other areas of research and innovation.
		Landscape Candidate Vaccines	TPP Vaccines	Trial design Vaccines	Simple protocol available	Regulatory pathway consultations	Landscape Candidate Therapeutics	TPP Therapeutics	Trial design Therapeutics	Simple protocol available	Regulatory pathway consultations	Landscape Candidate Diagnostics	TPP Diagnostics	Trial design Diagnostics	Simple protocol available	Regulatory consultations	
COVID-19	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓
MERS-CoV	✓	✓	✓	✓		✓	✓		✓			✓	✓				✓
Zika	✓	✓	✓	✓	✓	✓	✓	✓				✓	✓	✓		✓	✓
Nipah	✓	✓	✓	✓					✓	✓							✓
Lassa fever	✓	✓	✓	✓		✓	✓	✓	✓		✓	✓	✓	✓		✓	✓
Ebola ZEBV	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓
Ebola SUDV	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓
Marburg	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓			✓	✓
Crimean-Congo hemorrhagic fever	✓	✓	✓	✓		✓	✓	✓	✓		✓	✓	✓			✓	✓
Rift Valley fever	✓	✓	✓	✓		✓	✓		✓		✓	✓	✓				✓
Chikungunya	✓	✓	✓	✓			✓		✓								✓
Plague	✓	✓	✓	✓		✓	✓		✓		✓					✓	
Mpox	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓
Pathogen X	✓			✓					✓								

Global collaborative research approach to prevent and tackle outbreaks, epidemics and pandemics



Many countries across the globe participated in WHO-coordinated research activities between ¹⁷ May 22 and May 2023. Activities have been diverse and include a range of countries that took part in large global clinical trials to test vaccines and treatments for COVID-19.

Activities and outputs of the global research community to prevent and combat outbreaks and pandemics

144

The number of peer reviewed publications generated

775

(estimate)

The number of global conferences, meetings and training sessions held

Delivered between May 2022 and May 2023 and coordinated by the WHO R&D Blueprint

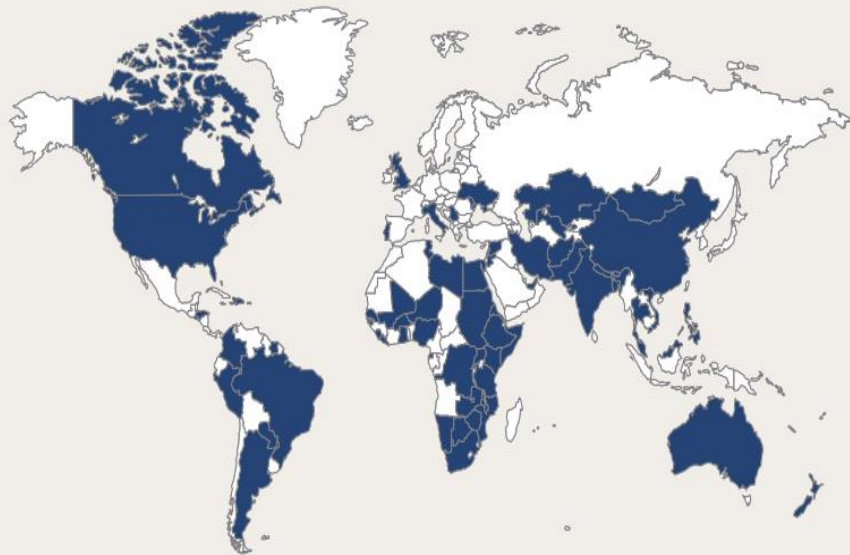
96

The number of WHO publications, reviews and assets produced

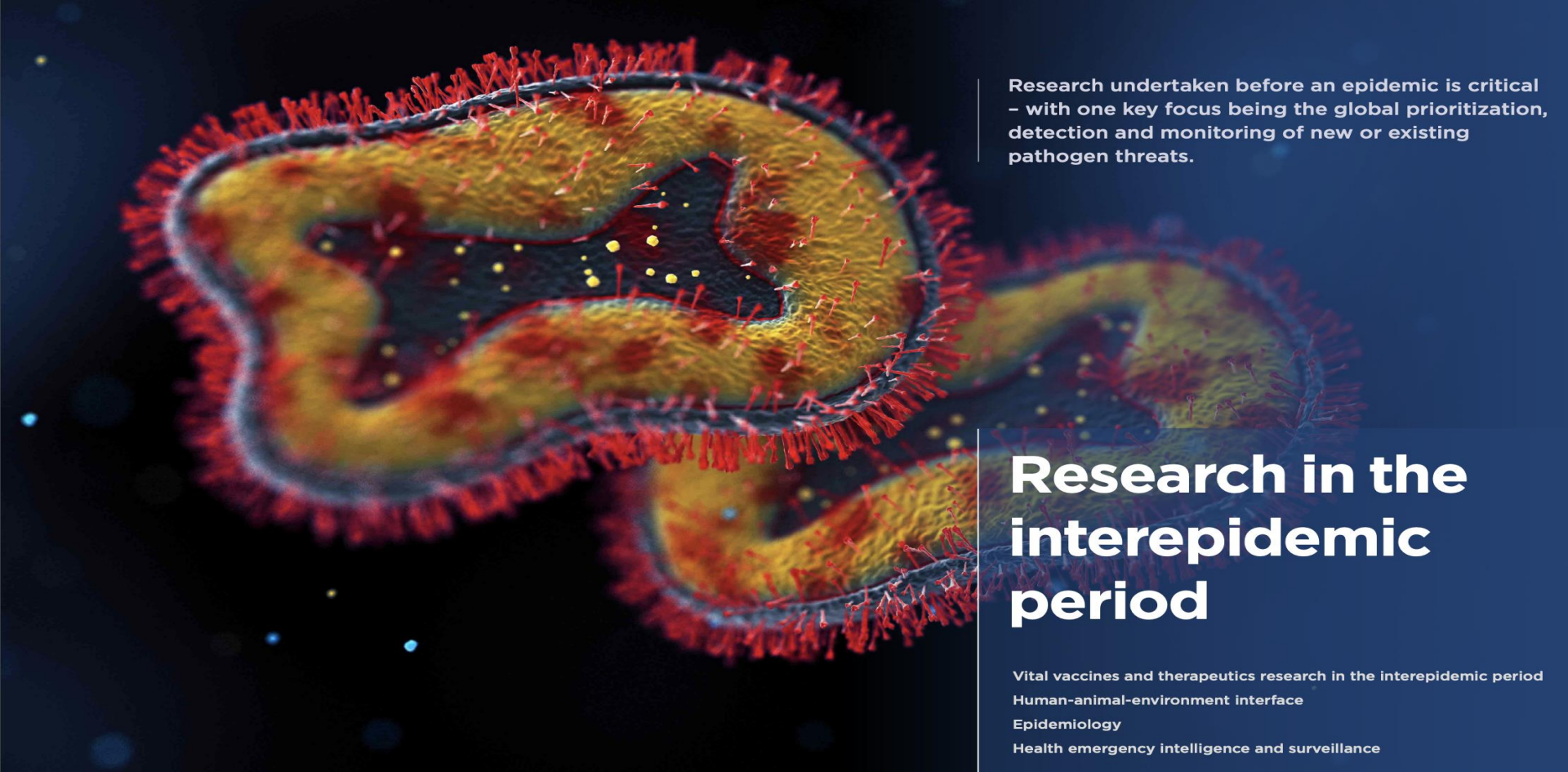
56,212

(estimate)

The number of global scientists, researchers and policy, engagement and regulatory experts that have participated in the events outlined above



■ Countries that participated in research activities, coordinated by WHO, to prevent or combat outbreaks and pandemics between May 2022 and May 2023



Research undertaken before an epidemic is critical – with one key focus being the global prioritization, detection and monitoring of new or existing pathogen threats.

Research in the interepidemic period

Vital vaccines and therapeutics research in the interepidemic period

Human-animal-environment interface

Epidemiology

Health emergency intelligence and surveillance



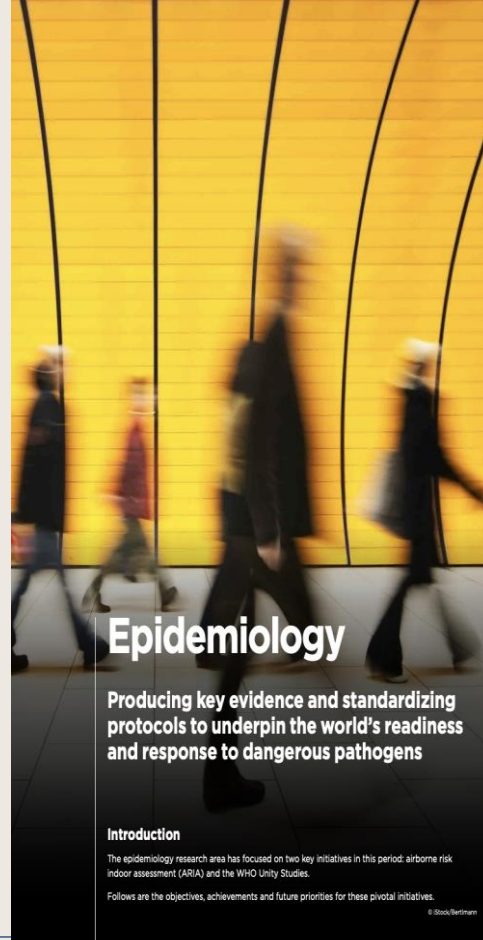
Vital vaccines and therapeutics research in the interepidemic period

Building protection and readiness in preparation for outbreaks



Human-animal-environment interface

The interaction of humans, animals and the environment in a changing world



Epidemiology

Producing key evidence and standardizing protocols to underpin the world's readiness and response to dangerous pathogens

Introduction

The epidemiology research area has focused on two key initiatives in this period: airborne risk indoor assessment (ARIA) and the WHO Unity Studies.

Follows are the objectives, achievements and future priorities for these pivotal initiatives.

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Health emergency intelligence and surveillance





During a disease outbreak, different plans and strategies across all the research areas are rapidly enacted.

A core focus of this phase is delivering major clinical trials of promising vaccines and treatments quickly and robustly.

Research integrated in the outbreak response

Vital vaccines and therapeutics research in the outbreak response	48
Clinical management	54
Infection prevention and control (IPC)	58
Public health and social measures (PHSM)	62



Vital vaccines and therapeutics research in the outbreak response

At the heart of the global response against deadly outbreaks

© WHO/Unilever



Clinical management

Optimizing clinical management of COVID-19 patients and clinical care in large-scale health emergencies



Infection prevention and control (IPC)

Readiness and response research and innovation (RI) for public health emergencies



Public health and social measures (PHSM)

Providing global evidence on the effectiveness and impact of PHSM for emergency preparedness and response

The delivery of effective medical countermeasures and wider policies to combat a disease outbreak is underpinned by a wide range of research areas. They all coordinate and work together enabling the global research effort before and during an outbreak.

Enabling research

Regulatory science	70
Biological standardization	74
Ethics	78
Community-centred readiness and response	82
Tackling infodemics	86
WHO Initiative on Trust and Pandemic Preparedness	90
Good participatory practice (GPP-EP)	94



Regulatory science

Regulatory systems are integral to the public health response: working together to accelerate equitable access to vital medical products



Biological standardization

Helping increase access to life-saving vaccines, treatments and diagnostics



Ethics

Prioritizing pivotal ethics work before and during pandemics and outbreaks



Community-centred readiness and response

Data driving action



Tackling infodemics

Promoting a resilient and healthier
information environment

WHO Initiative on Trust and Pandemic Preparedness



Good participatory practice for clinical trials of new or re-emerging pathogens (GPP-EP)

Evidence-driven community engagement
in clinical trials



Building on the global research response to the pandemic to combat the next one

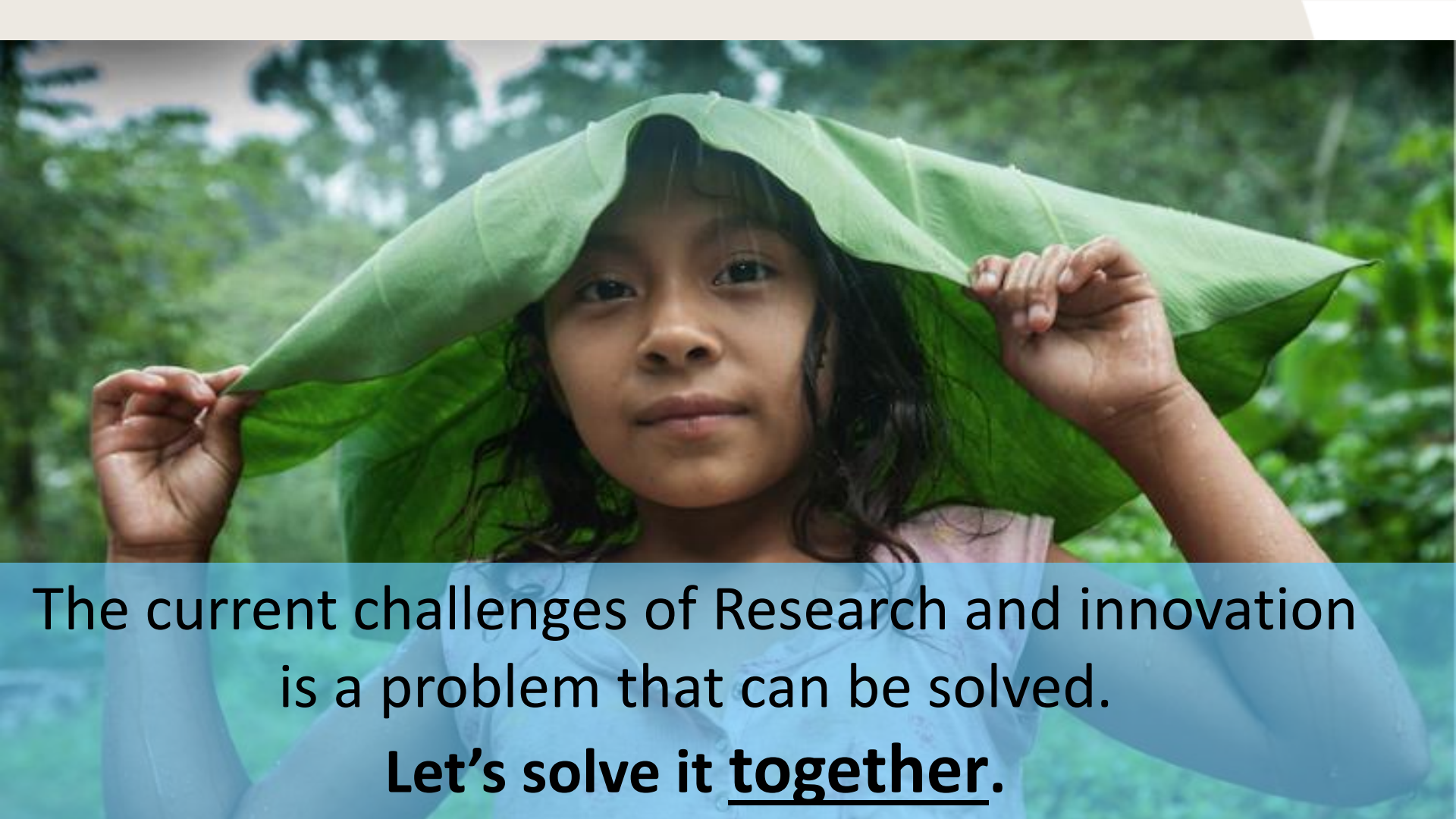
On behalf of thousands of colleagues across the three levels of WHO, we would like to thank the over 50,000 researchers and Ministries of Health officials who have joined our efforts; the funders who have facilitated critical research; and the thousands of volunteers who have generously contributed to the studies worldwide.

Global Research and Innovation for Health Emergencies

**Building the world's resilience against
future outbreaks and pandemics**

October 2023





The current challenges of Research and innovation
is a problem that can be solved.

Let's solve it together.