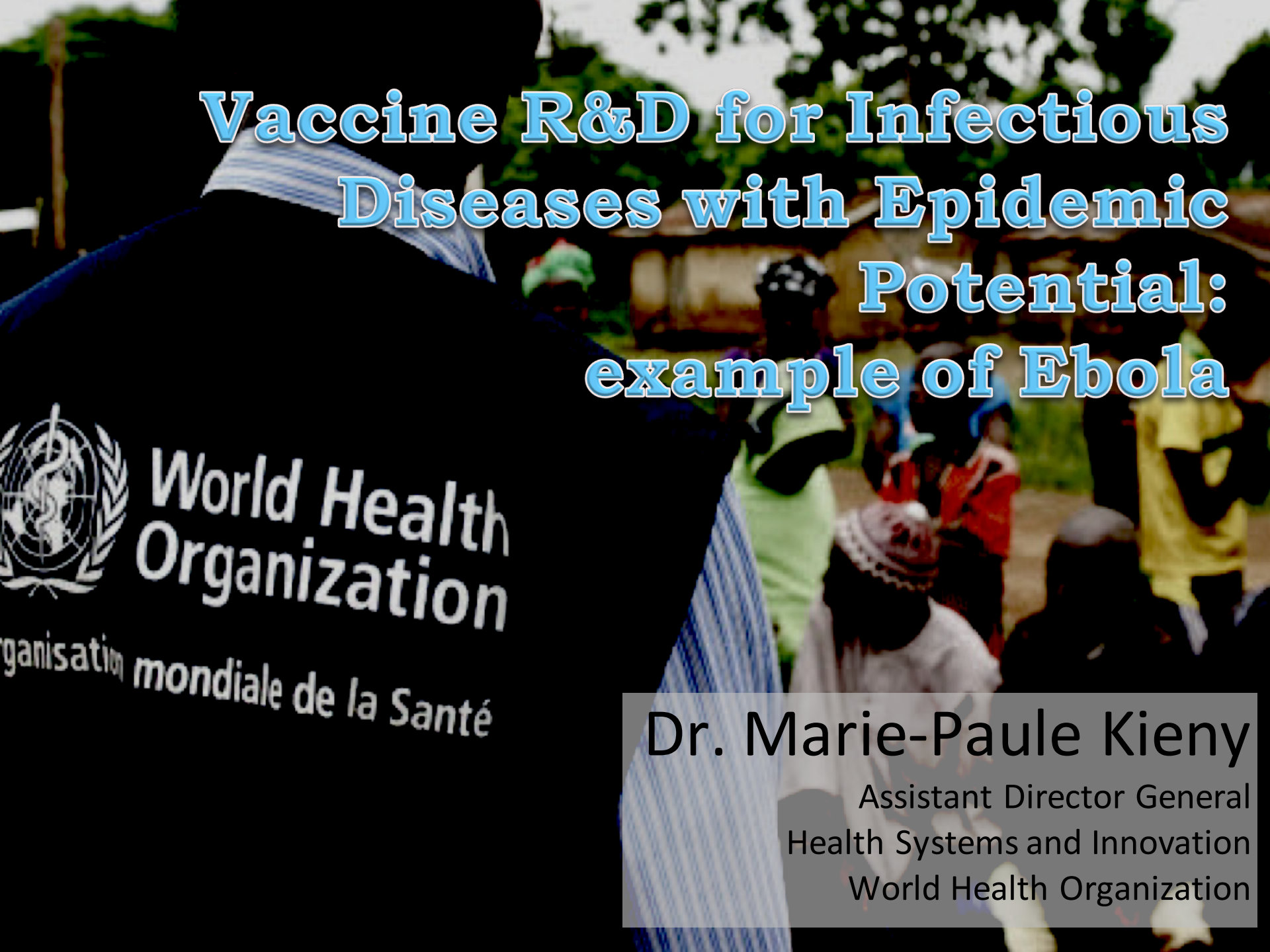


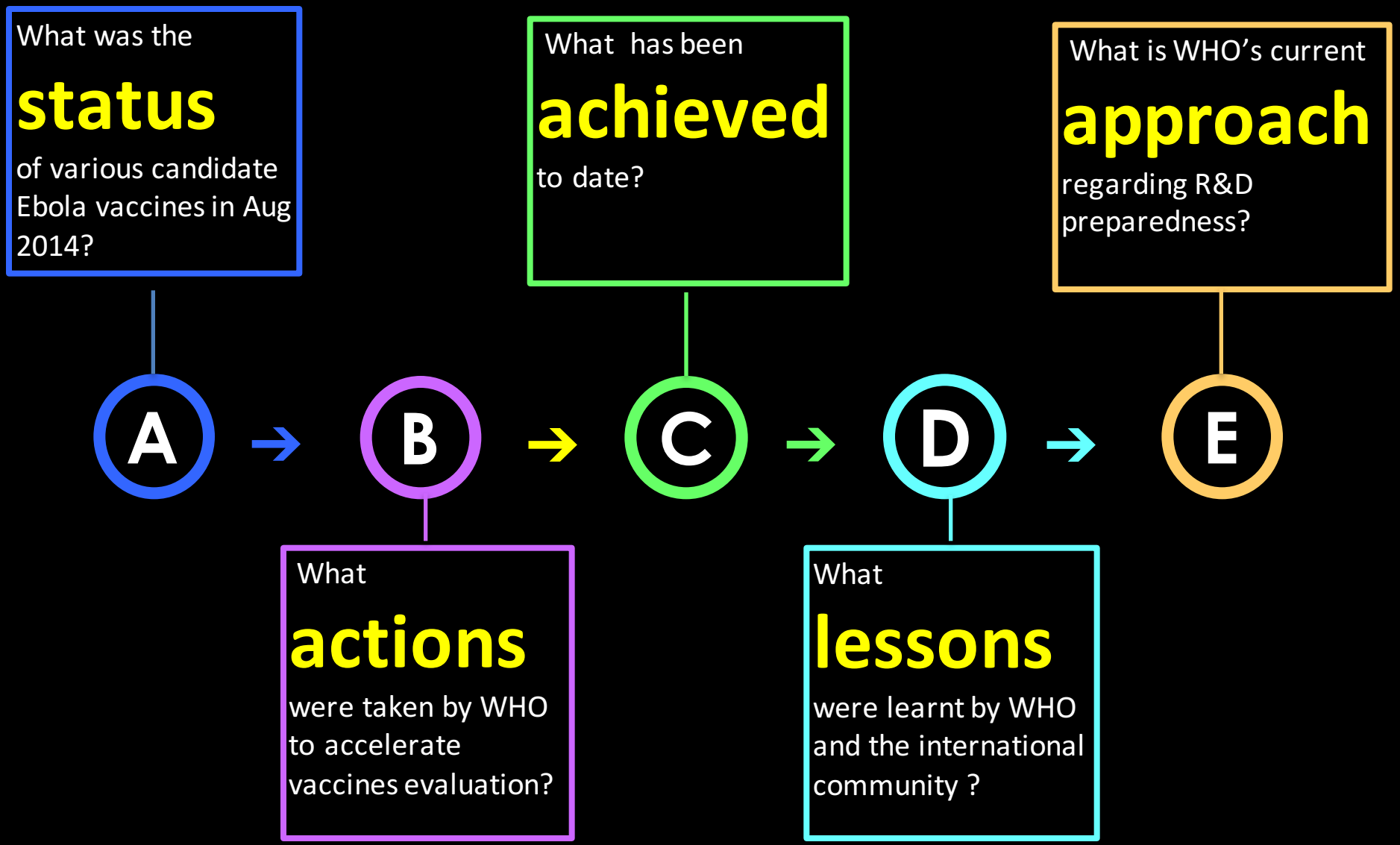
Vaccine R&D for Infectious Diseases with Epidemic Potential: example of Ebola

Dr. Marie-Paule Kieny

Assistant Director General
Health Systems and Innovation
World Health Organization

8 August 2014

WHO declared a public health emergency of international concern



World Health Organization

What was the

status

of various candidate Ebola vaccines in Aug 2014?

A

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Ebola vaccines pipeline in Aug 2014…

NON- CLINICAL EVAL.

CLINICAL EVALUATION

Protein Sciences CORPORATION

VLP

Profectus BioSciences, Inc.

rVSV

Jefferson THOMAS JEFFERSON UNIVERSITY

Rec. rabies

VAXART

Ad5

J&J

Ad26/MVA

gsk

ChAd3

NewLink GENETICS

MERCK Be well

rVSV-ΔG

World Health Organization

B

What

actions

were taken by WHO to accelerate vaccines evaluation?

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3 questions driving the global efforts

1. Are these vaccines efficacious & are they safe?
2. Can they be evaluated more rapidly in order that they might be moved from the laboratory to the field?
3. Can they be scaled up to serve the necessary demand and contribute to outbreak control?

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What has been

achieved

to date?

C

World Health Organization

Ebola vaccines in clinical development

Vaccine	Multivalent/ monovalent	Antigen and strain	Strategy	Phase
ChAd3.EBOZ	Monovalent	GP from Mayinga 1976 EBOV	One dose	Phase 2
rVSV.EBOV	Monovalent	GP from Kikwit EBOV strain	One dose	Phase 3
Ad26.ZEBOV	Monovalent	GP from Mayinga strain EBOV	Prime-boost	Phase 2b
MVA BN Filo	Multivalent	GP from EBOV, SUDV, Marburg and NP from TAFV		
GP VLP	Monovalent	GP from Makona 2014 EBOV	One dose	Phase 1
rAd5.EBOV	Monovalent	GP from Guinea 2014 EBOV	High dose single dose	Phase 1b
DNA plasmid (EBODNA023-00-VP)	Bivalent	GP from Mayinga 1976 EBOV, Gulu 1977 SUDV strain	Two doses	Phase 1b
VSV-EBOV	Monovalent		Prime-boost	Registered in Russia
rAd5-EBOV	Monovalent			

EBOV, Ebolavirus Zaire species; GP, glycoprotein; MVA, Modified Vaccinia Ankara; NP, nucleoprotein; SUDV, Ebolavirus Sudan species; TAFV, Taï Forest virus; VLP, virus-like particle.
Source: Sridhar S 2015

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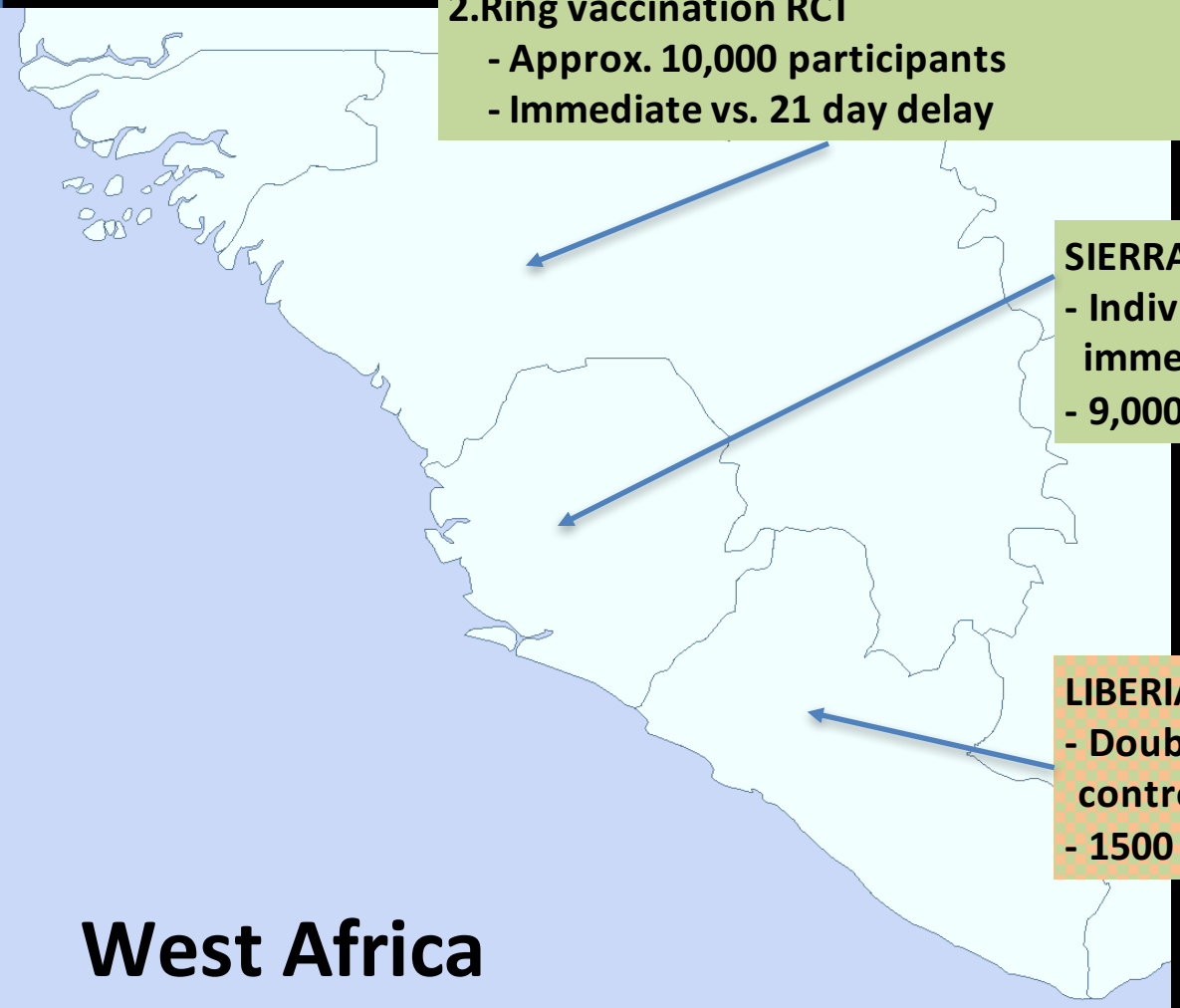
Sites of Ebola vaccine Phase 3 trials



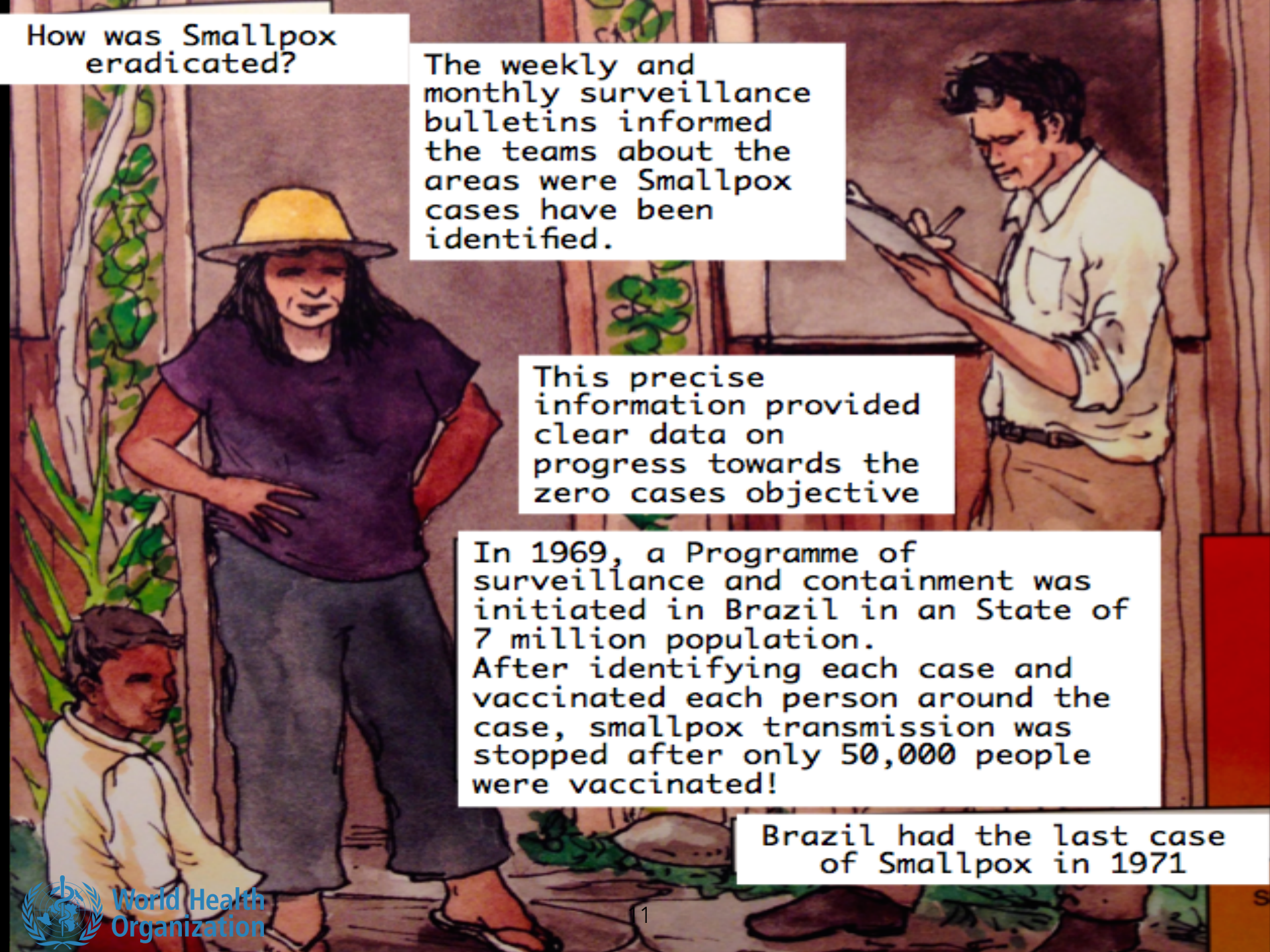
GUINEA, "Ebola ça suffit" (rVSV-ZEBOV)
1. Cohort study among Front Line Worker - Approx. 3,500 participants
2. Ring vaccination RCT
   - Approx. 10,000 participants
   - Immediate vs. 21 day delay

SIERRA LEONE, "STRIVE" (rVSV-ZEBOV)
- Individually randomized (un-blinded) to immediate vs delayed arm
- 9,000 health care workers

LIBERIA, "PREVAIL" rVSV/ChAd3/Placebo)
- Double blinded, individually randomized controlled
- 1500 individuals at risk

West Africa

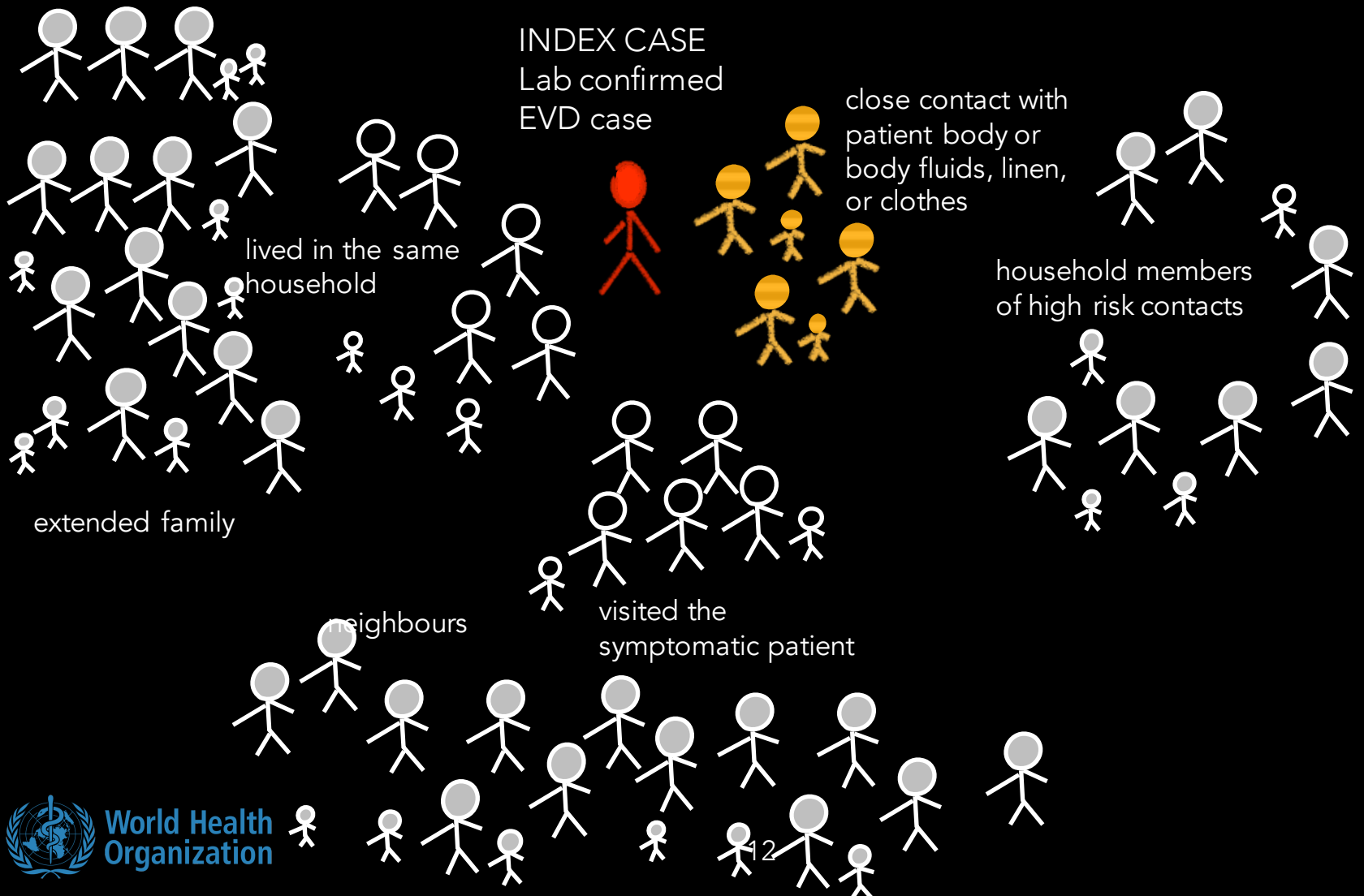
World Health Organization



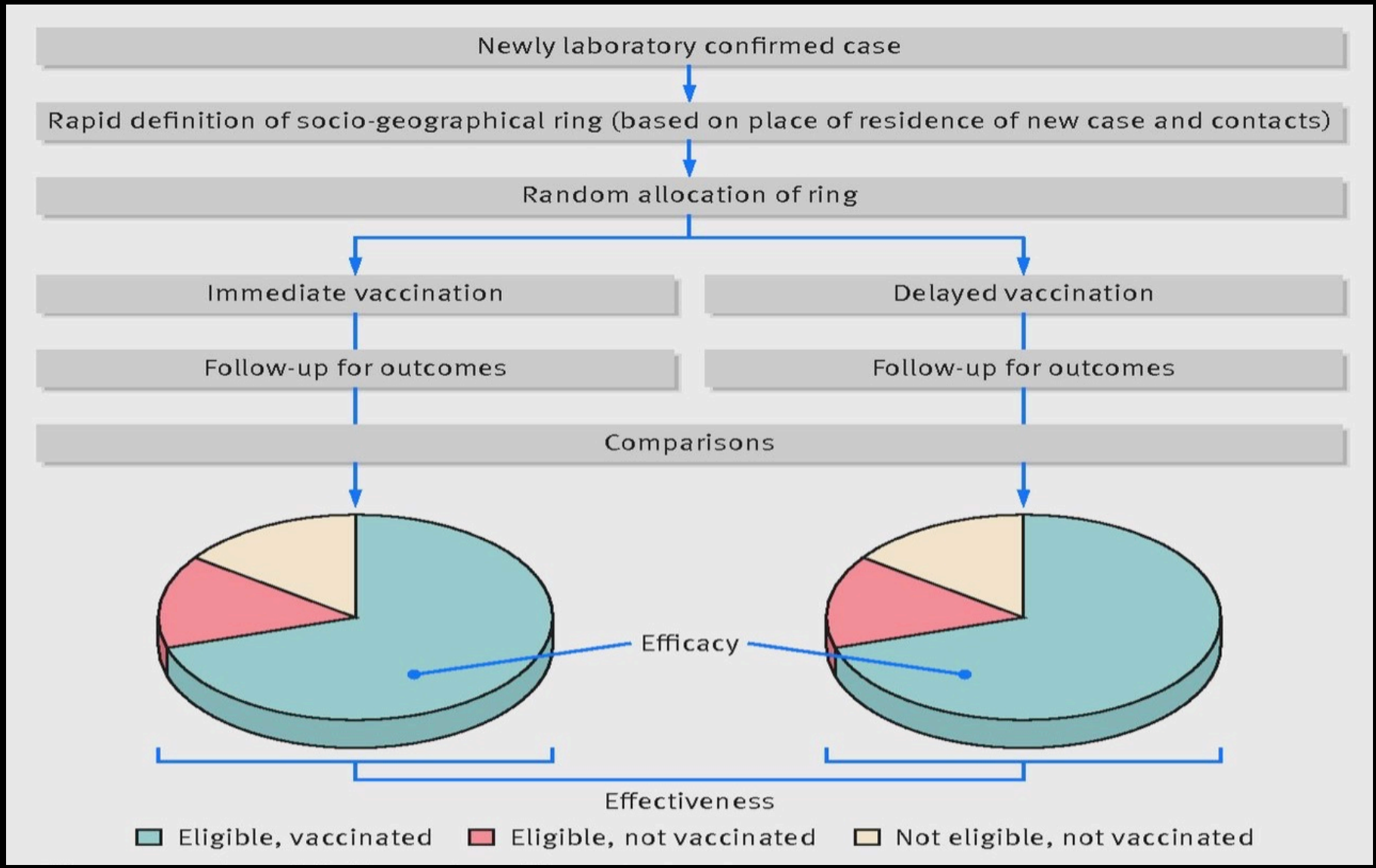
World Health Organization

What is a vaccination ring?

Contacts and contacts of contacts



Schematic presentation of the design of a ring vaccination trial



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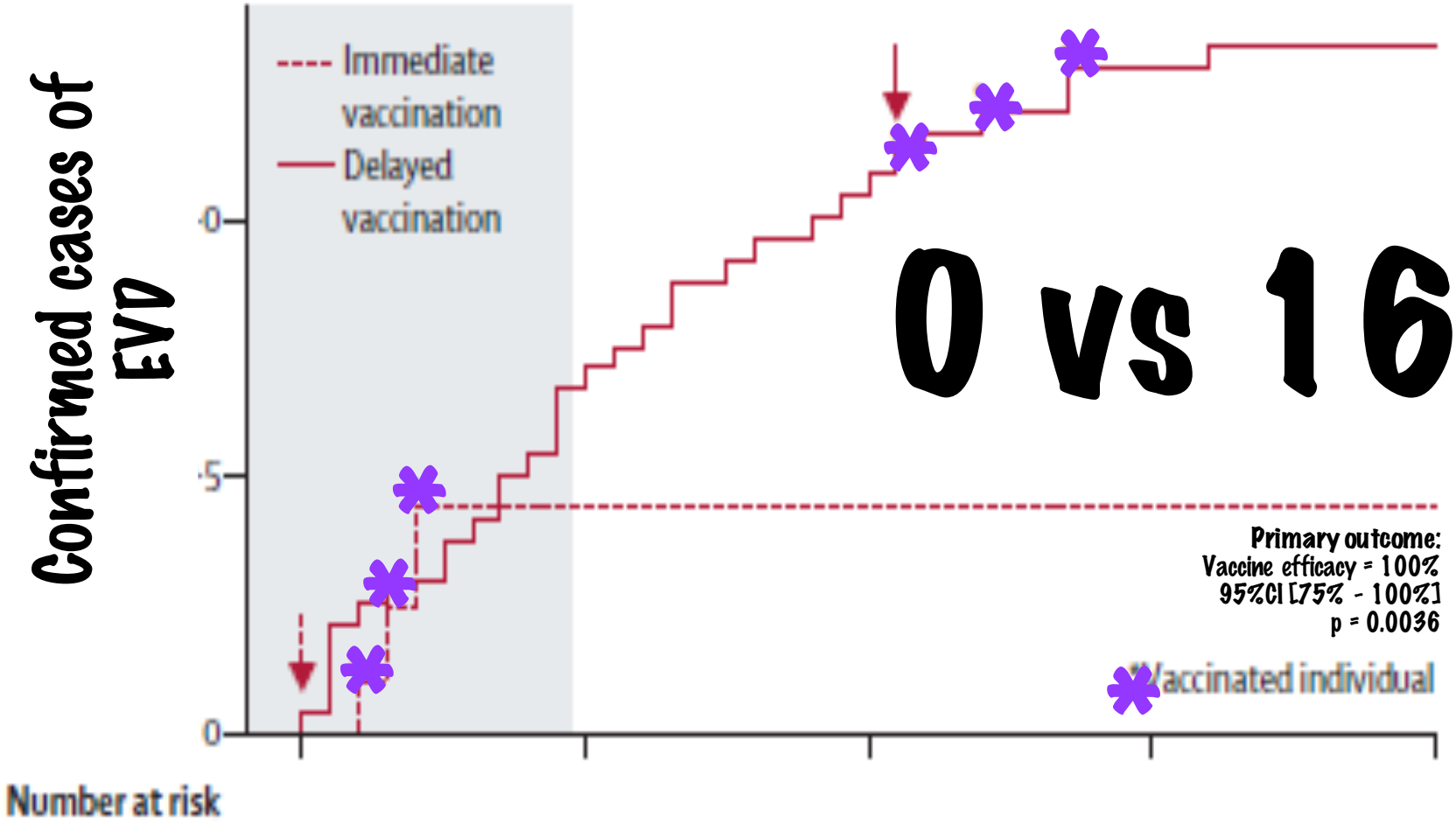
In the ring vaccination trial, teams go to communities with a recently confirmed Ebola case

World Health Organization

Four months later, preliminary results on efficacy were disseminated and the trial data help inform a public health intervention to control the disease

All vaccinated in immediate rings versus all eligible in delayed vaccination rings



The p value needed to declare success in interim analysis was 0·0027, a level that the interim primary analysis (p=0·0036) did not meet.

Ebola vaccines safety summary

- No serious adverse events vaccine related
- Reactive arthritis cases identified as an adverse event in Geneva VSV Phase 1 trial. Spontaneous resolution with good prognosis.
- Safety data from Phase 1 studies of both ChAd3 and rVSV vaccines indicate an acceptable safety profile in healthy adults and children older than 5 years of age.
- No data are currently available regarding the safety of these vaccines in subjects with underlying disease or medical conditions.
- There are also no data regarding the safety of these products in younger children and pregnant subjects.
- Ongoing studies will provide additional experience in adults, and will allow more extensive assessment of safety.

Source : GACVS report June 2015

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Ebola vaccines immunological summary

Despite that a correlate of protection has not been defined, one dose of rVSV and high dose of ChAd3 results in good levels of antibody titres.

These immune responses are enhanced in prime-boost regimes using MVA-based virus vectors as a boosting vaccination, although the optimal interval between the priming and boosting vaccination is not known.

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Ebola vaccines - efficacy summary

Ring trial Guinea

The preliminary results suggest that the experimental vaccine against the Ebola virus (rVSV-ZEBOV) is capable of protecting the vaccinated people (after an anticipated delayed of approximately 10 days)

None of the more than 10 000 participants who have been vaccinated to date (in randomized or not randomised vaccination rings) have developed EVD after 9 days or more after vaccination.

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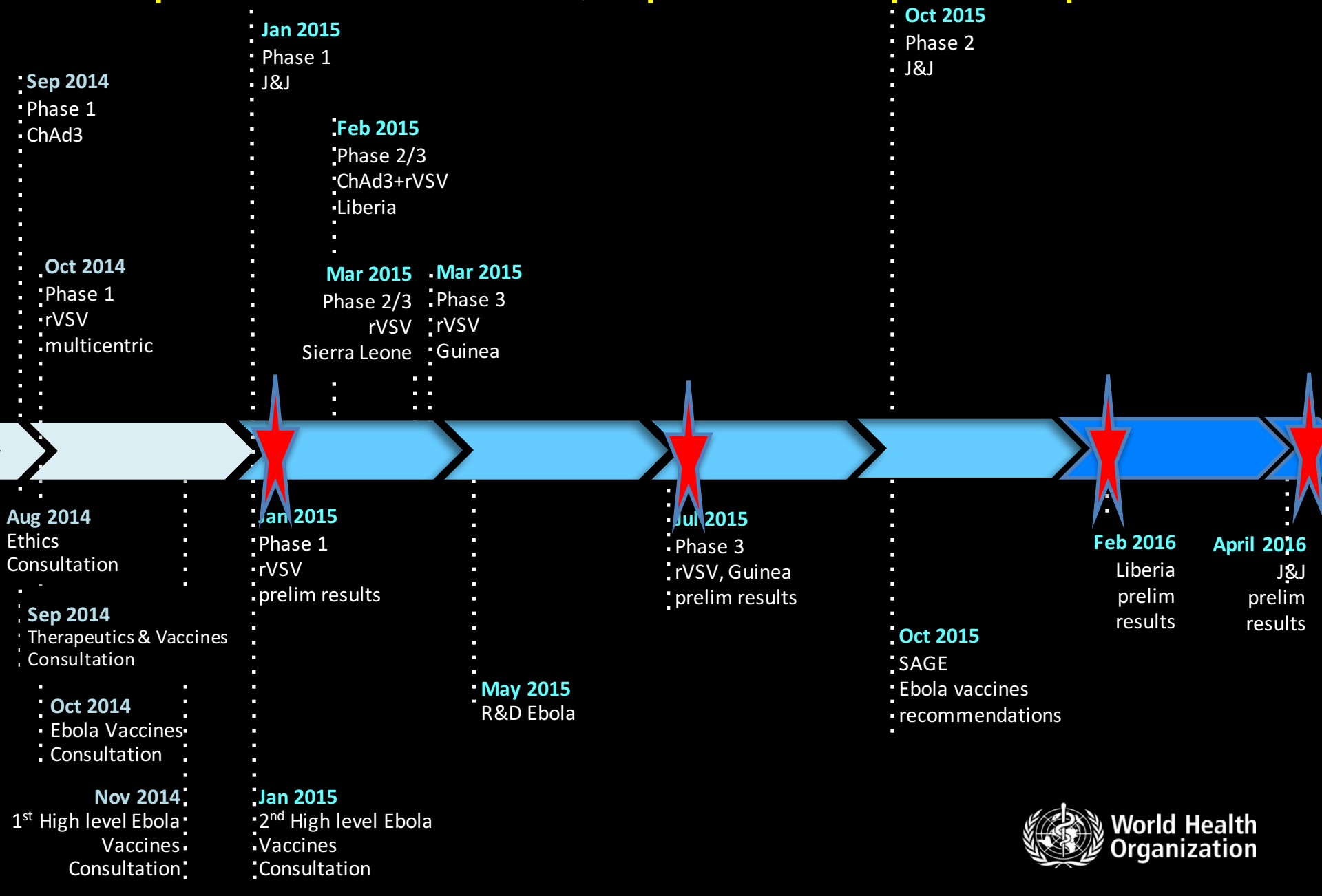
Collaborative efforts, adaptation of the traditional R&D model, compressed timeframes and, unprecedented partnerships formed



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Ebola vaccines pipeline now…

NON- CLINICAL EVAL.

CLINICAL EVALUATION

Protein Sciences CORPORATION

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Rec. rabies

VAXART

Ad5

RESEARCH INSTITUTE OF INFLUENZA · MINISTRY OF HEALTHCARE OF THE RUSSIAN FEDERATION

Ad26/MVA

Rec. Influenza

NOVAVAX Creating Tomorrow's Vaccines

VLP

ChAd3

CanSinotech ink ICS Be well

rVSV-ΔG

RUSAL

Russian vaccine

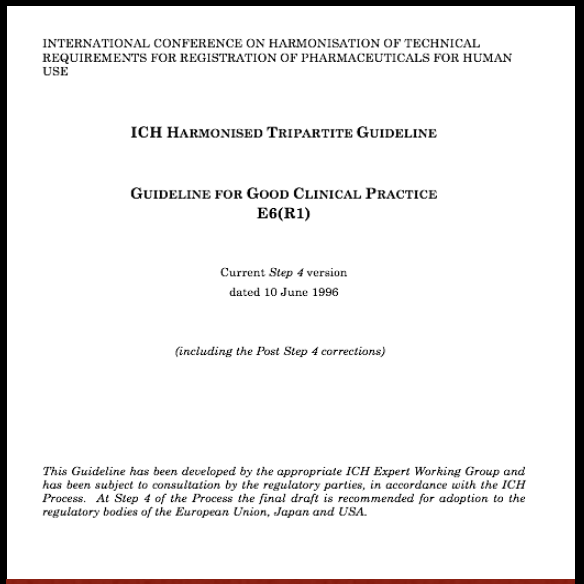
World Health Organization

Emerging data from candidate Ebola vaccines

Response to flare-ups using rVSV-EBOV

Vaccination using an unlicensed vaccine means extra vigilance as compared with using a licensed vaccine:

- participants must be informed of the risk of taking an experimental vaccine and must sign informed consent and;
- providers must conduct the vaccination in compliance with Good Clinical Practice



INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED TRIPARTITE GUIDELINE

GUIDELINE FOR GOOD CLINICAL PRACTICE
E6(R1)

Current *Step 4* version
dated 10 June 1996

(including the Post Step 4 corrections)

This Guideline has been developed by the appropriate ICH Expert Working Group and has been subject to consultation by the regulatory parties, in accordance with the ICH Process. At Step 4 of the Process the final draft is recommended for adoption to the regulatory bodies of the European Union, Japan and USA.

Nearly 2000 people have been vaccinated under expanded access in Sierra Leone and Guinea

D

What

lessons

were learnt by WHO and the international community ?

World Health Organization

The Ebola epidemic has demonstrated that **it is possible to accelerate R&D during emergencies** and that it is feasible to safely and effectively implement research interventions in an affected country.

It also highlighted the **imperative to advance R&D preparedness** and effective collaboration frameworks in advance of any new epidemic.

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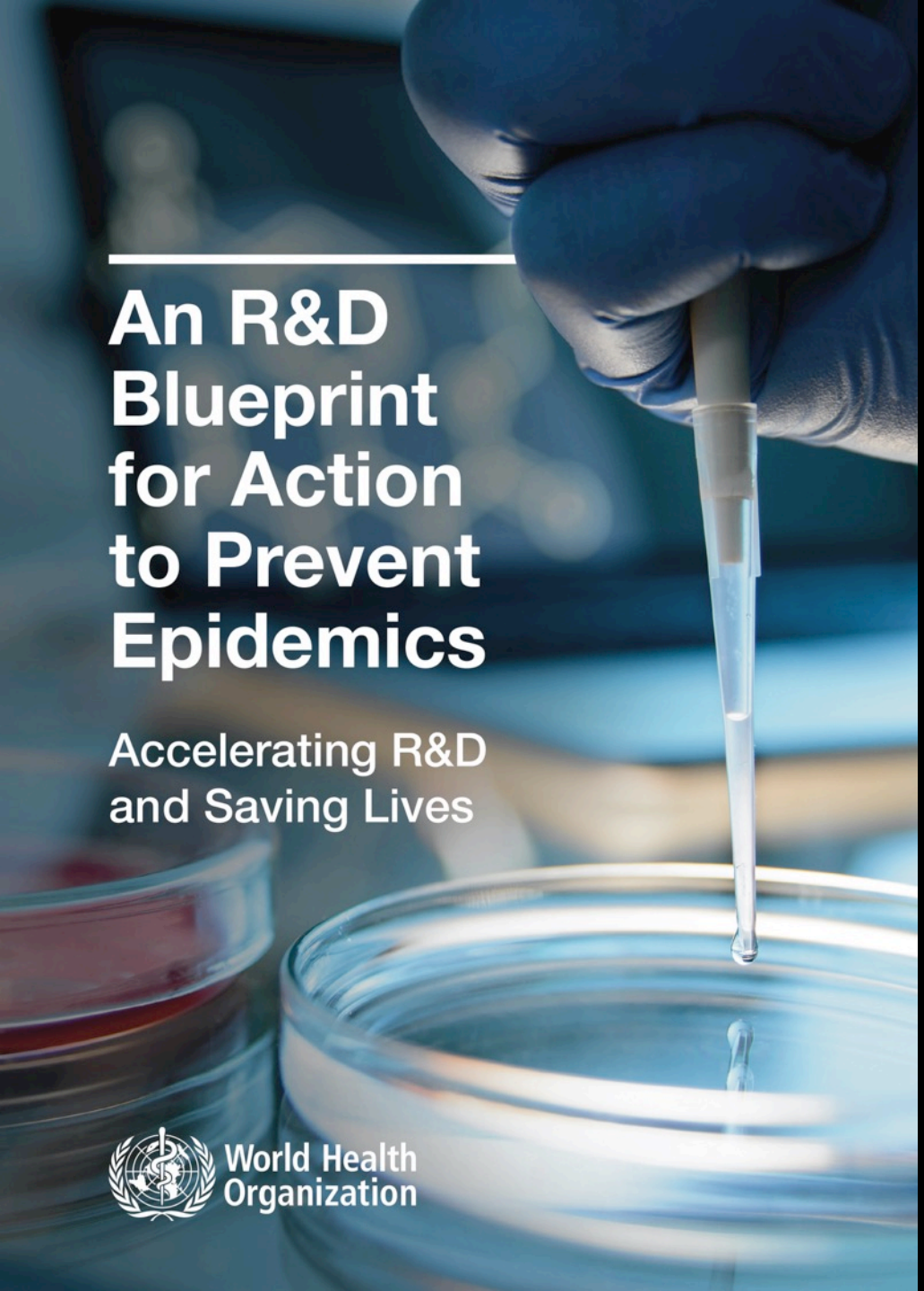

An R&D Blueprint for Action to Prevent Epidemics

Accelerating R&D and Saving Lives

World Health Organization

WHO's proposal regarding R&D preparedness

E

World Health Organization

Approaches currently being used to improve preparedness under the R&D Blueprint.

A — Improving coordination & fostering an enabling environment

1. Building an effective governance & coordination framework
2. Outlining innovative transparent and aligned funding processes
3. Encouraging effective communication

B — Accelerating Research & Development processes

1. Assessing epidemic threat & defining priority pathogens
2. Developing R&D roadmaps to accelerate evaluation of diagnostics, therapeutics & vaccines
3. Outlining appropriate regulatory & ethical pathways

C — Developing new norms and standards adapted to the epidemic context

1. Supporting expansion of capacity to implement adequate study designs
2. Developing guidance & tools to frame collaborations and exchanges
3. Anticipating evidence needs to inform regulatory review and policy development

World Health Organization

What would success look like?

The Blueprint aims to reduce the time between the declaration of a public health emergency of international concern and the availability of effective tests, vaccines and medicines that can be used to save lives and avert crisis.

The R&D Blueprint represents WHO's new start for a better R&D preparedness.

The current lack of R&D preparedness is a problem that can be solved.

Let's solve it together!

World Health Organization