# An R&D Blueprint for action to prevent epidemics

Report to the Scientific Advisory Group

8-9 February 2017

# Why an R&D Blueprint?

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.

# Operational objective of the Blueprint


The R&D Blueprint seeks to create an enabling environment through which all actors, through increased funding, data sharing and partnerships, can drive change in the public health landscape to provide an elevated level of global impact.

# Ebola vaccine efficacy trial

THE LANCET

Online First Current Issue All Issues Special Issues Multimedia Information for Authors

All Content Search Advanced Search

< Previous Article Volume 389, No. 10068, p505–518, 4 February 2017 Next Article >

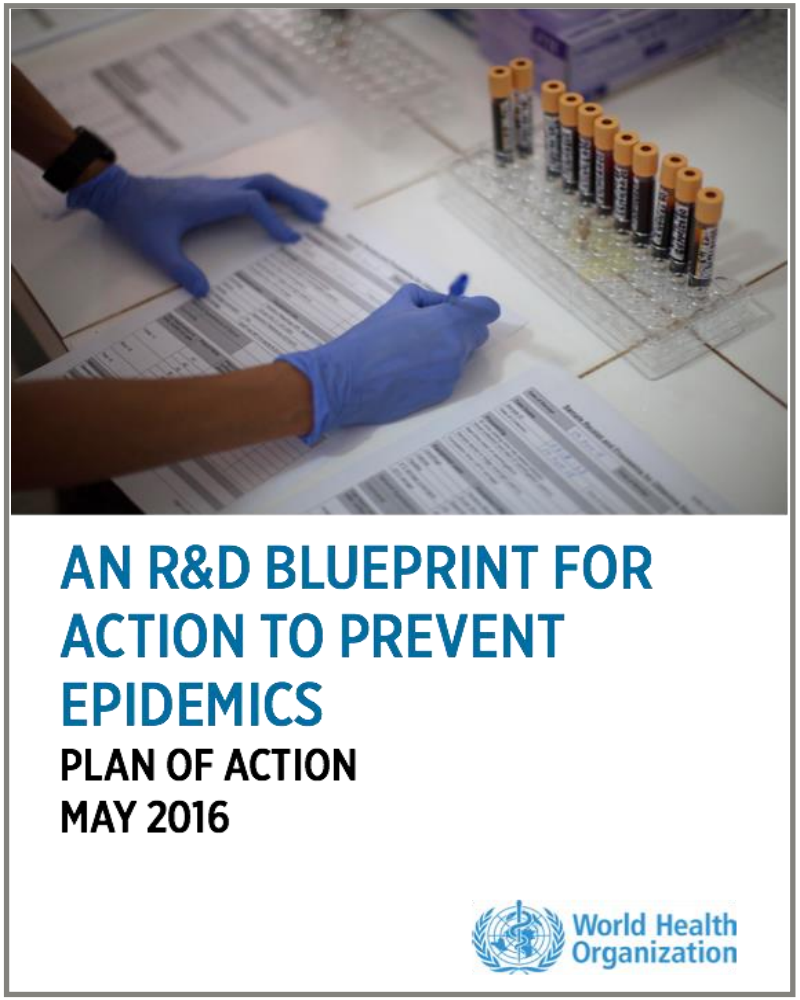
Articles

## Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ça Suffit!)

Dr Ana Maria Henao-Restrepo, MD, Anton Camacho, PhD, Prof Ira M Longini, PhD, Conall H Watson, MFPH, Prof W John Edmunds, PhD, Prof Matthias Egger, PhD, Miles W Carroll, PhD, Natalie E Dean, PhD, Ibrahima Diatta, MSc, Moussa Doumbia, MD, Bertrand Draguez, MD, Sophie Duraffour, PhD, Godwin Enwere, FWACP, Rebecca Grais, PhD, Stephan Gunther, MD, Pierre-Stéphane Gsell, PhD, Stefanie Hossmann, MSc, Sara Viksmoen Watle, MD, Prof Mandy Kader Kondé, PhD, Sakoba Kéïta, MD, Souleymane Kone, MSc, Eewa Kuisma, PhD, Prof Myron M Levine, MD, Sema Mandal, MD, Thomas Mauget, MBA, Gunnstein Norheim, PhD, Ximena Riveros, MSc, Aboubacar Soumah, MD, Sven Trelle, MD, Andrea S Vicari, PhD, Prof John-Arne Røttingen, MD†, Marie-Paule Kieny, PhD†

† Contributed equally

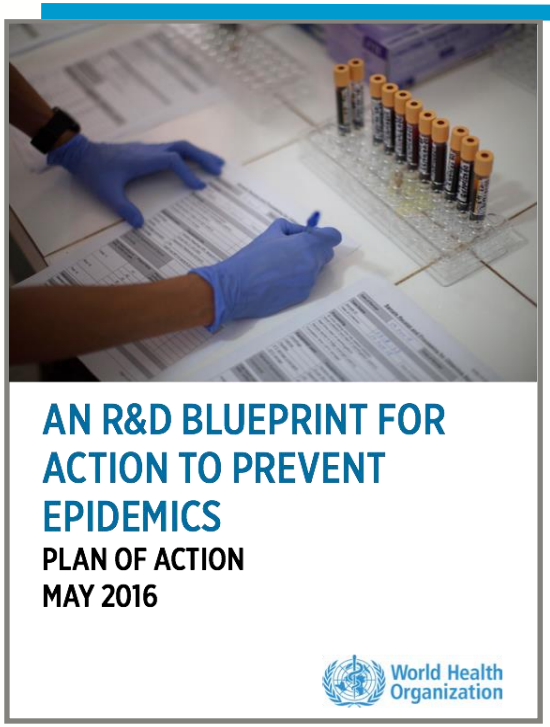
# What is the Blueprint?




- a global **strategy** and preparedness **plan**
- a **convening mechanism** and an **instrument** to articulate technical guidance

# The Blueprint approaches are aligned with:

- the lessons learned during the 2014–2016 Ebola epidemic and
- the recommendations of the various reviews on the Ebola epidemic conducted to date




# 4 principles

**1**

An inclusive process with a clear mandate and defined milestones

**2**

Building on the efforts of others in the community

**3**

A collaborative effort with the Member States in the affected countries at the core of it

**4**

Driven by scientific knowledge

# Approaches to improve preparedness under the R&D Blueprint

**A** Improving coordination & fostering an enabling environment

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

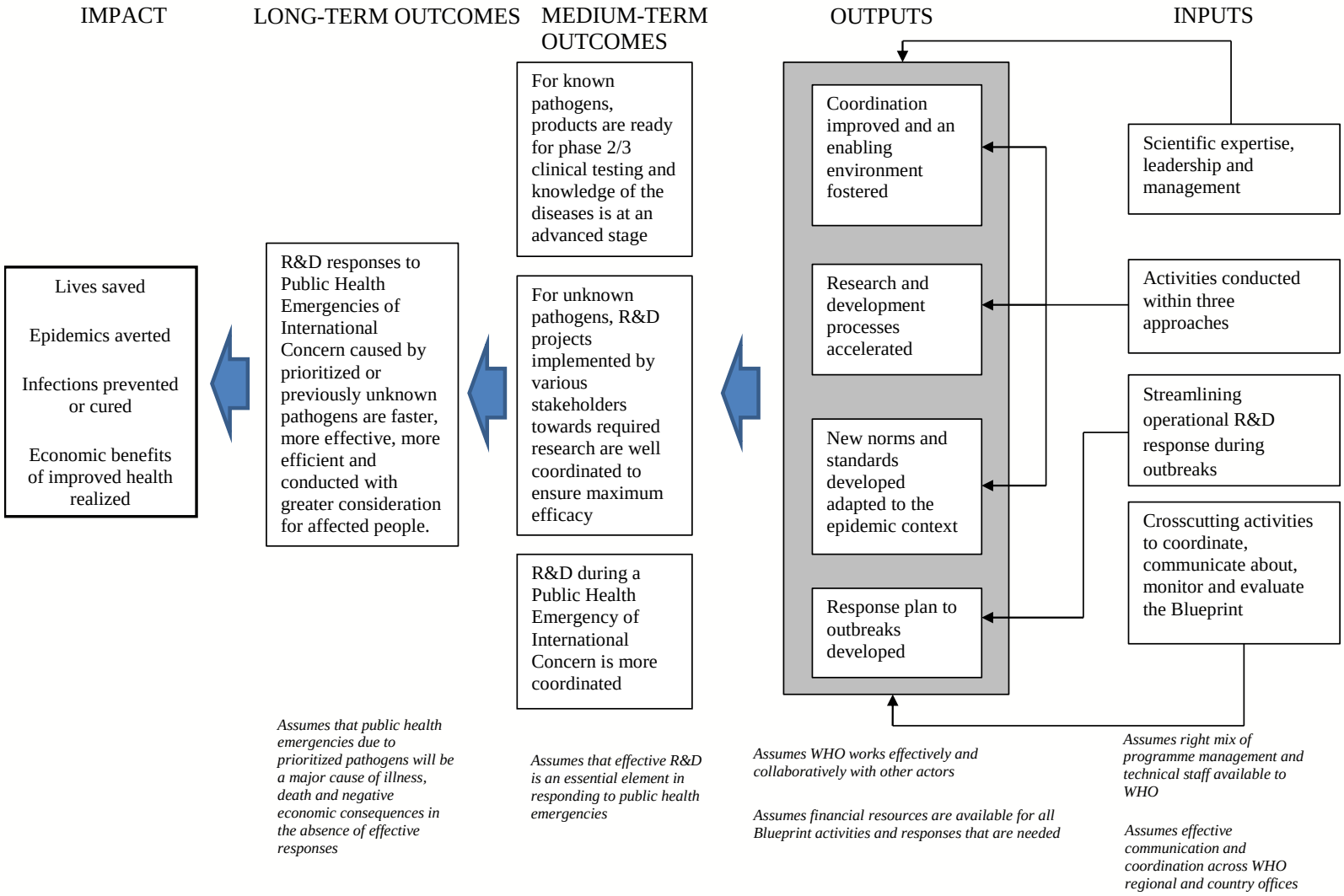
**B** Accelerating Research & Development processes

1. Assessing epidemic threat & defining priority pathogens
2. Developing R&D roadmaps to accelerate evaluation of Dx, therapeutics & vaccines
3. Outlining 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
3. Anticipating evidence needs for regulatory review and policy development

# Monitoring the impact



# Operationalizing the Blueprint

**Steering Group**
2 WHO Clusters HIS, FWC and WHE programme Management team

**Scientific Advisory Group**

**HIS**
Priority pathogens
Regulatory & ethical pathways
TPPs/data sharing/MTAs
Monitoring & Evaluation
Financial Admin
Blueprint Communication

**FWC**
Global coordination
Roadmaps
Clinical trials capacity

**WHE**
R&D plans during outbreaks

# Main recent achievements

**A** Improving coordination & fostering an enabling environment

- Steps to create the Global Coordination Framework

**B** Accelerating Research & Development processes

- Revised list of prioritized pathogens
- MERS-CoV roadmap
- TPPs for Zika, MERS-CoV, Ebola
- EUAL procedure
- Zika R&D response
- Identification of potential platform technologies

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

- ICMJE guidelines for sharing results
- Steps to inform discussions on trial designs
- Developing MTA capacity building tool

# An expanding network of partners and collaborators

- Observer on the GloPID-R assembly
- Collaboration with CEPI

- Invaluable support and inputs from numerous partners including:
  - Wellcome Trust
  - BARDA, NIH, CDC, Chatham House, Inst Pasteur
  - MSF, UNICEF
  - BMGF
  - FDA, EMA
  - Numerous academic institutions: U of Florida, LSHTM, U of Laval, U of Texas, EmLab …..

# WHO Principles for engaging with CEPI

## An MoU to frame the collaboration

- Any vaccine coming out of CEPI's efforts will be **available to and affordable** for those in need;
- The price of the vaccine coming out of CEPI's efforts will be **delinked from the costs of R&D**;
- Collaboration will be based on an **open** basis;
- IP will be managed in a manner which **maximizes access**;
- CEPI will be **transparent and open to all actors**, large and small, from the North and the South. Funding will be based on merit;
- As CEPI will be based on public and philanthropic funding, it will operate on a "shared benefit" basis.

Due diligence under **FENSA** was conducted and collaboration with CEPI was authorized.


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.

# The WHO Research & Development Blueprint

Scientific Advisory Group meeting

8-9 February 2017

# *Improving coordination and fostering an enabling environment*

Report to the R&D Blueprint Scientific Advisory Group

Geneva, 8-9 February 2017

R&D BLUEPRINT

# A Improving coordination & fostering an enabling environment

R&D BLUEPRINT

## Building an effective governance & coordination framework

Formalise and get operational a mechanism for improved and coordinated R&D preparedness and response capacity

Start mapping of key stakeholders to have an overview of existing initiatives & stakeholders

Scoping meeting Global Coordination Mechanism

2015 2016 2017

Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 BEYOND

## Outlining innovative transparent and aligned funding processes

Consultation with stakeholders & identification of funding options

Average funding needs estimated

Report of financial options finalised and published

2015 2016 2017

Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 BEYOND

## Encouraging effective communicatio

Blueprint SAG and other consultations

ZIKA open

Develop a template framework to streamline global stakeholder collaboration

Scientific interactions: Zika, Mers-Cov, … …

2015 2016 2017

Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 BEYOND

Centre on Global Health Security
Meeting Summary

CHATHAM HOUSE
The Royal Institute of International Affairs

# Establishing a Global Coordination Mechanism for Research and Development to Prevent and Respond to Epidemics: Scoping Meeting

**November 2016**

A first scoping meeting co-hosted by Chatham House, the Wellcome Trust and WHO brought together key stakeholders in global R&D

R&D BLUEPRINT

World Health Organization

# A Global Coordination Mechanism

**The Nature of Global R&D Coordination**

The primary role of a coordinating mechanism would be to address the global R&D agenda in a collaborative manner in order to ensure that identified R&D gaps are being filled effectively.

To be successful, the coordination mechanism would need a consensual governance framework to which key stakeholders have adhered.

A high-level continuum between coordination and governance would be needed in order bridge the recognised misalignments in R&D preparedness and response

# A Global Coordination Mechanism

**The Scope of the Coordination Mechanism**

The WHO Blueprint Plan of Action focus primarily on R&D activities associated with the development and availability of medical countermeasures.

Coordination during emergencies can only be successful if it builds on established coordination.

Therefore, coordination should take place throughout preparedness, in getting relevant actors together, as well as during public health emergency operations.

# A Global Coordination Mechanism

## Activities 2017

All agreed that a Global Coordination Mechanism (GCM) led by WHO was needed.

**March 28, 2017 -** A further meeting will be convened in to review the proposed scope and terms of reference of the GCM and to agree on the establishment of the GCM.

Zika as a test case of the GCM.

**2nd Quarter 2017** - Complete visualization tools on existing networks and initiatives relevant to this work.

# A Improving coordination & fostering an enabling environment

R&D BLUEPRINT

Formalise and get operational a mechanism for improved and coordinated R&D preparedness and response capacity

## Building an effective governance & coordination framework

Start mapping of key stakeholders to have an overview of existing initiatives & stakeholders

Scoping meeting Global Coordination Mechanism

2015 2016 2017

Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 BEYOND

## Outlining innovative transparent and aligned funding processes

Consultation with stakeholders & identification of funding options

Average funding needs estimated

Report of financial options finalised and published

2015 2016 2017

Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 BEYOND

Blueprint SAG and other consultations

ZIKA open

Develop a template framework to streamline global stakeholder collaboration

Scientific interactions: Zika, Mers-Cov, … …

## Encouraging effective communicatio

2015 2016 2017

Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 BEYOND

## What are the anticipated benefits?

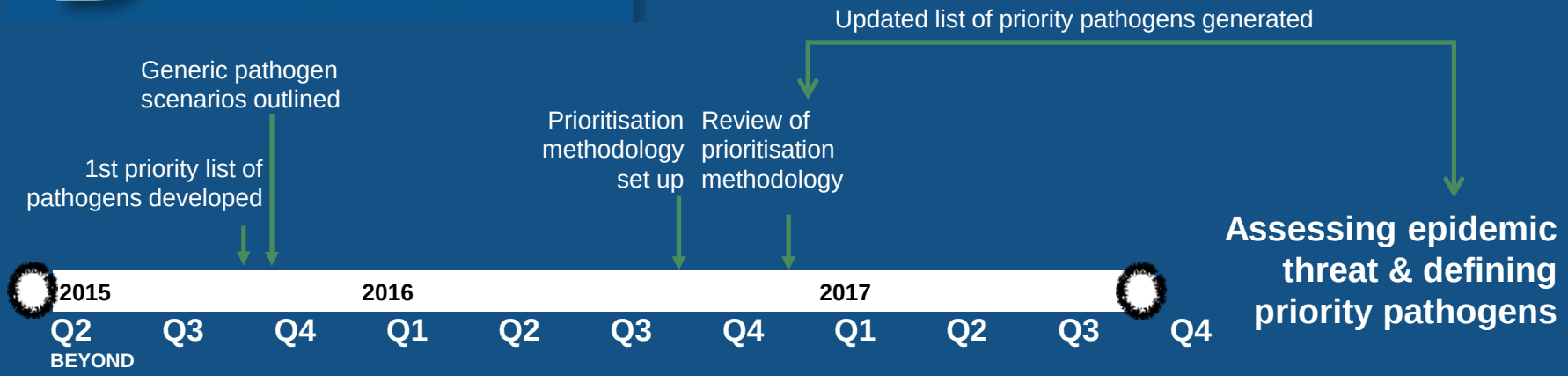
Global response efforts are faster, more consistent, transparent and better coordinated, with less waste and redundancy.

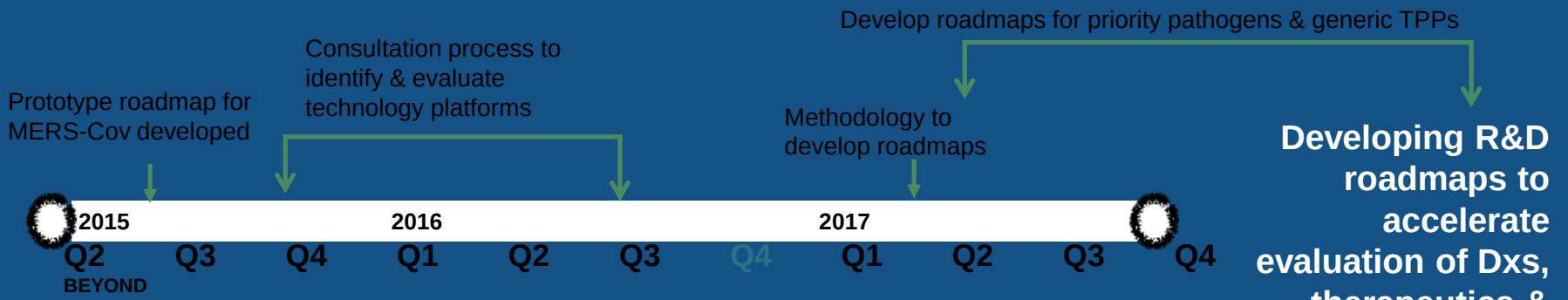
Ownership and buy-in from key stakeholders and communities are increased.

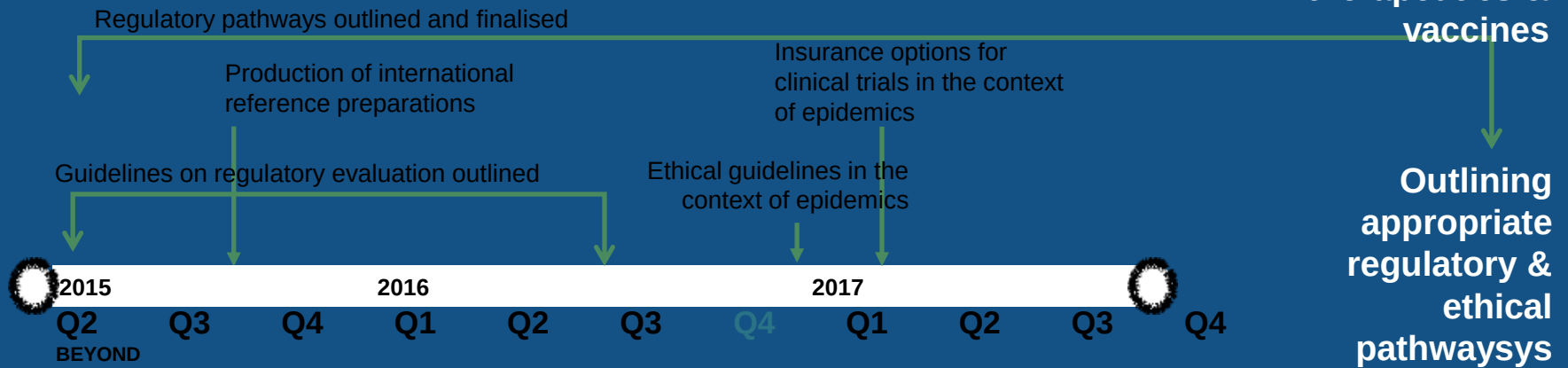
The enabling environment will allow effective, transparent and equitable collaboration between the contributing stakeholders to produce the desired result: an effective response to public health emergencies that is quick and efficient.

# Assessing epidemic threat and defining priority pathogens

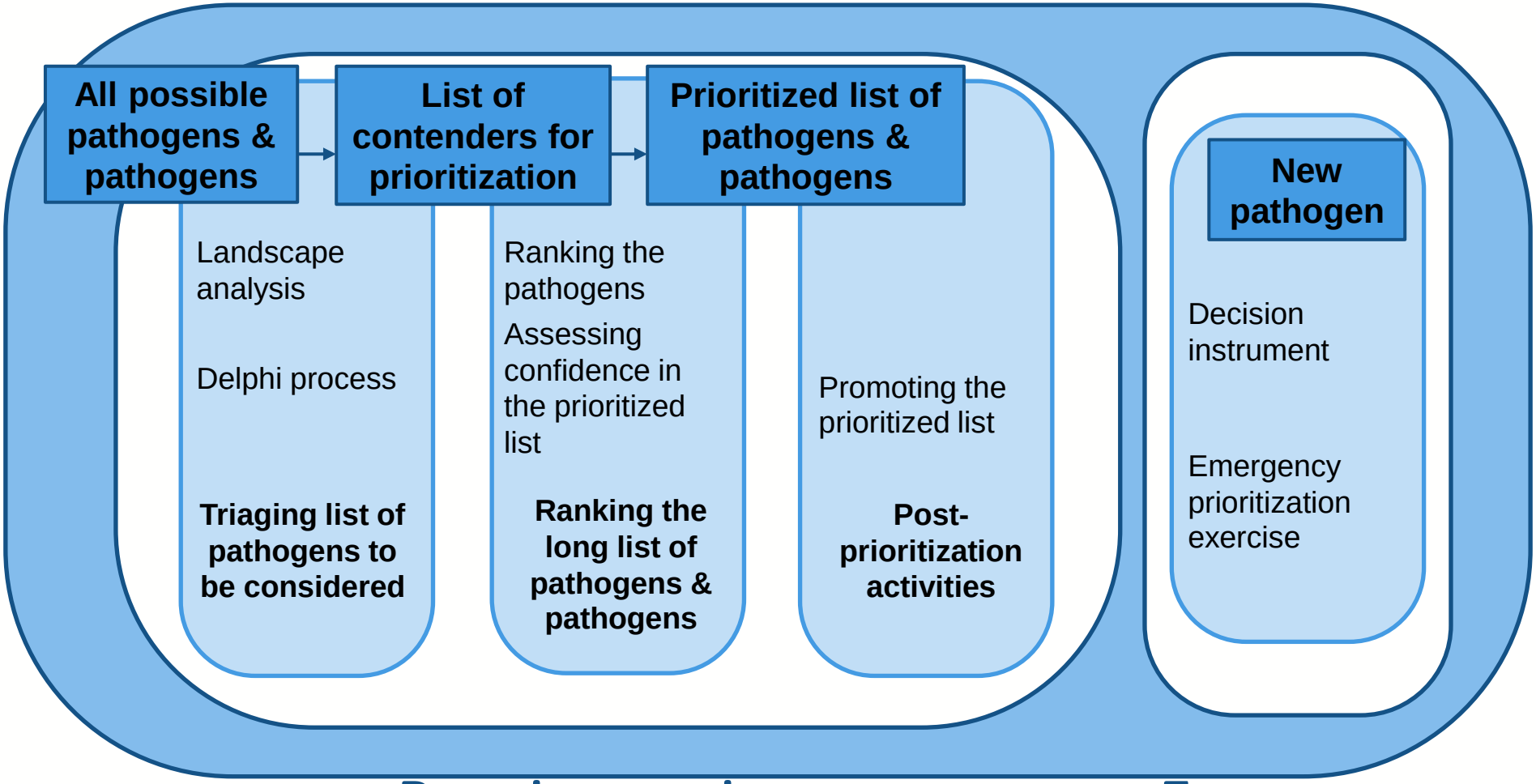
# B Accelerating Research & Development processes



# Overview of the prioritization process



# Timeline

## Activities undertaken to-date

**May 2015** – WHO international consultation on Blueprint

**December 2015** – WHO informal consultation on priority pathogens

**Early 2016** – Blueprint team develops methodology outline

**May 2016** – SAG reviews methodology outline

**Summer / Autumn 2016** – Detailed methodology developed

**December 2016** – Informal consultation reviews & validates methodology

**January 2017** – Annual review of list of priority pathogens

# Prioritization criteria

## Factors used to prioritize pathogens

| Criteria | Weights |
|---|---|
| Human transmissibility | 32% |
| Medical countermeasures | 21.90% |
| Severity | 14.65% |
| Human/animal interface | 9.42% |
| Other contributing factors | 9.42% |
| Public health context of the affected area | 6.13% |
| Potential social impacts | 4.18% |
| Evolutionary potential | 2.28% |

# List of priority pathogens 2017

(The order of pathogens on this list does not denote any ranking of priority)

- Lassa Fever and other severe Arenaviral haemorrhagic fevers
- Crimean Congo Haemorrhagic Fever
- Filoviral pathogens (including Ebola and Marburg)
- MERS-CoV
- Other high-path coronaviral pathogens (such as SARS)
- Nipah and related henipaviral pathogens
- Rift Valley Fever
- Severe fever with thrombocytopenia syndrome
- Zika

And any pathogen identified by the decision instrument

Chikungunya Virus continues to warrant further research and development.

# Other areas of substantial output

Other pathogens were considered & a wide range of additional relevant R&D initiatives encouraged

1. Emerging flaviviruses (such as Kyasanur Forest pathogen or Usutu);
2. Emerging Bunyaviruses (such as Oropouche);
3. Emerging Alphaviruses (such as Chikungunya & Mayaro virus);
4. Rickettsia;
5. Plague;
6. Hantaviral pathogens;
7. Chandipura virus pathogen.

- Cross-cutting R&D to address multiple pathogens
- One-Health approach
- Anti-microbial resistance

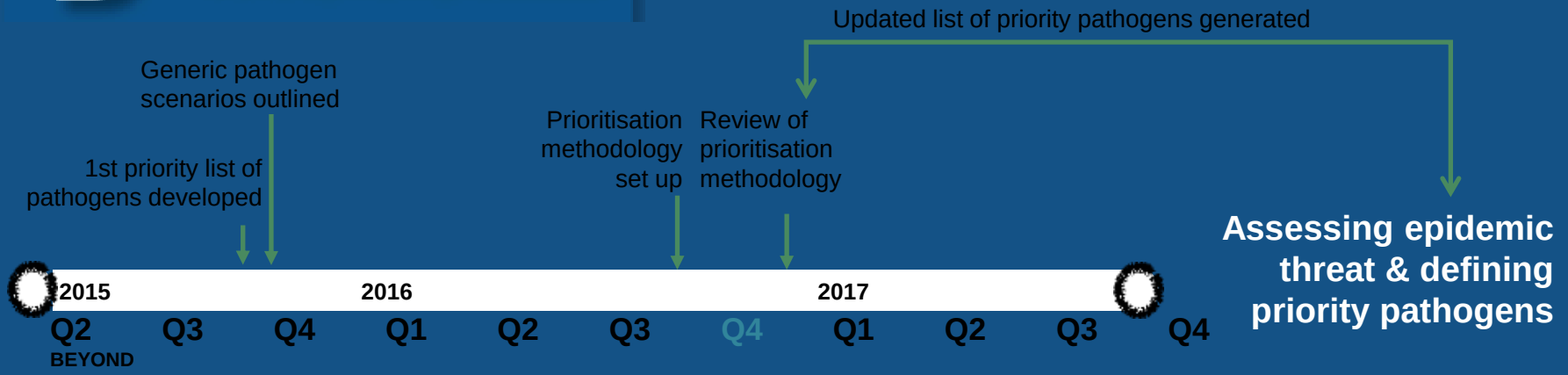
## What are the anticipated benefits?

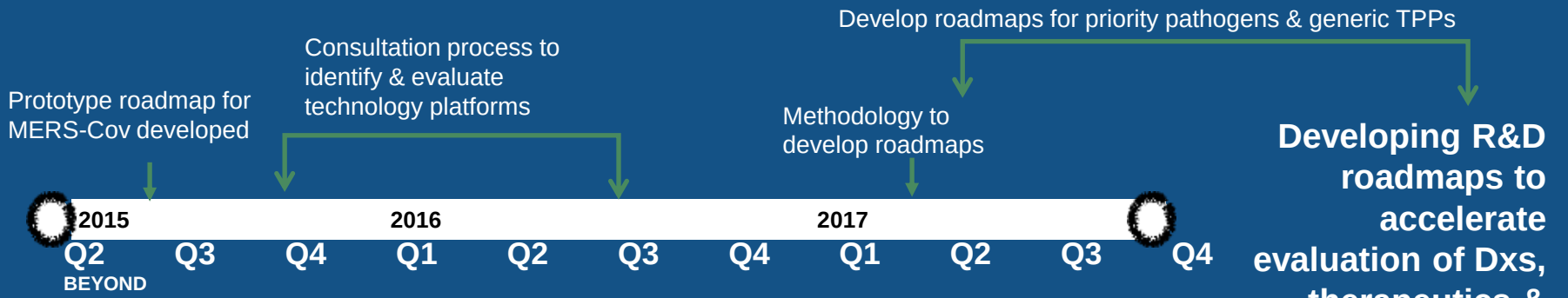
Factors that are important to identify priority pathogens are known.

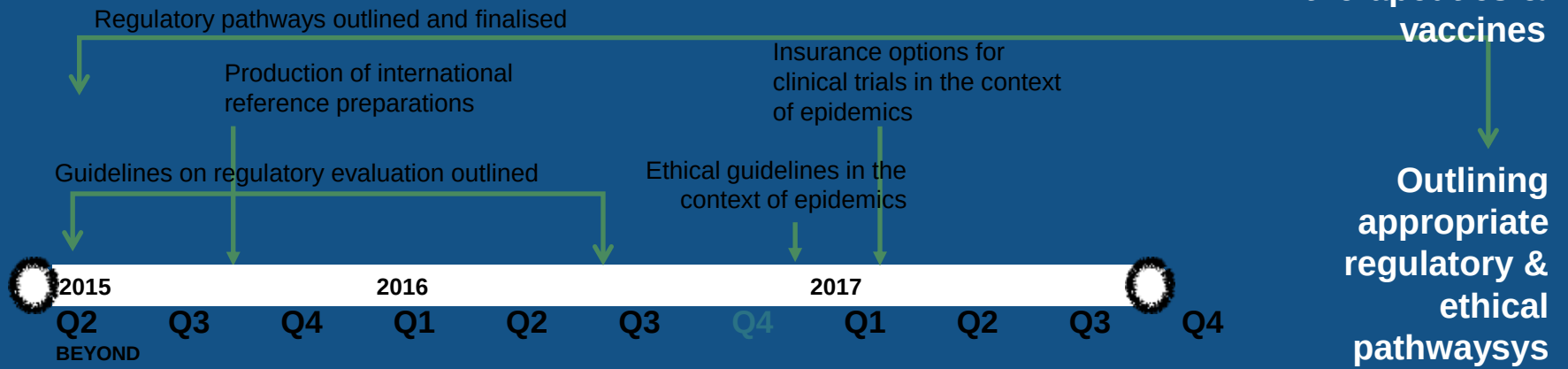
A decision tree for determining when a novel pathogen would trigger an interim prioritization assessment is available.

# R&D Blueprint Roadmaps

# B Accelerating Research & Development processes



# R&D Blueprint Roadmaps

WHO R&D Blueprint

## priority pathogens

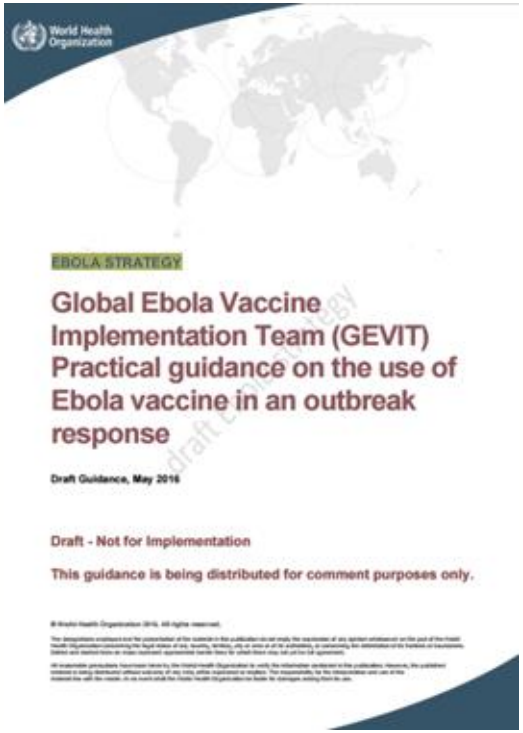
any necessary actions for such priority pathogens
coordinated through pathogen-specific initiatives

## design of R&D roadmaps

to accelerate evaluation of medical countermeasures
diagnostics, therapeutics and vaccines

## R&D Blueprint roadmaps

Vision, strategic goals and priorities towards accelerated R&D
from basic research through to late-stage development, licensure and *early use* of products
to prevent and control pathogens due to priority pathogens



# Context

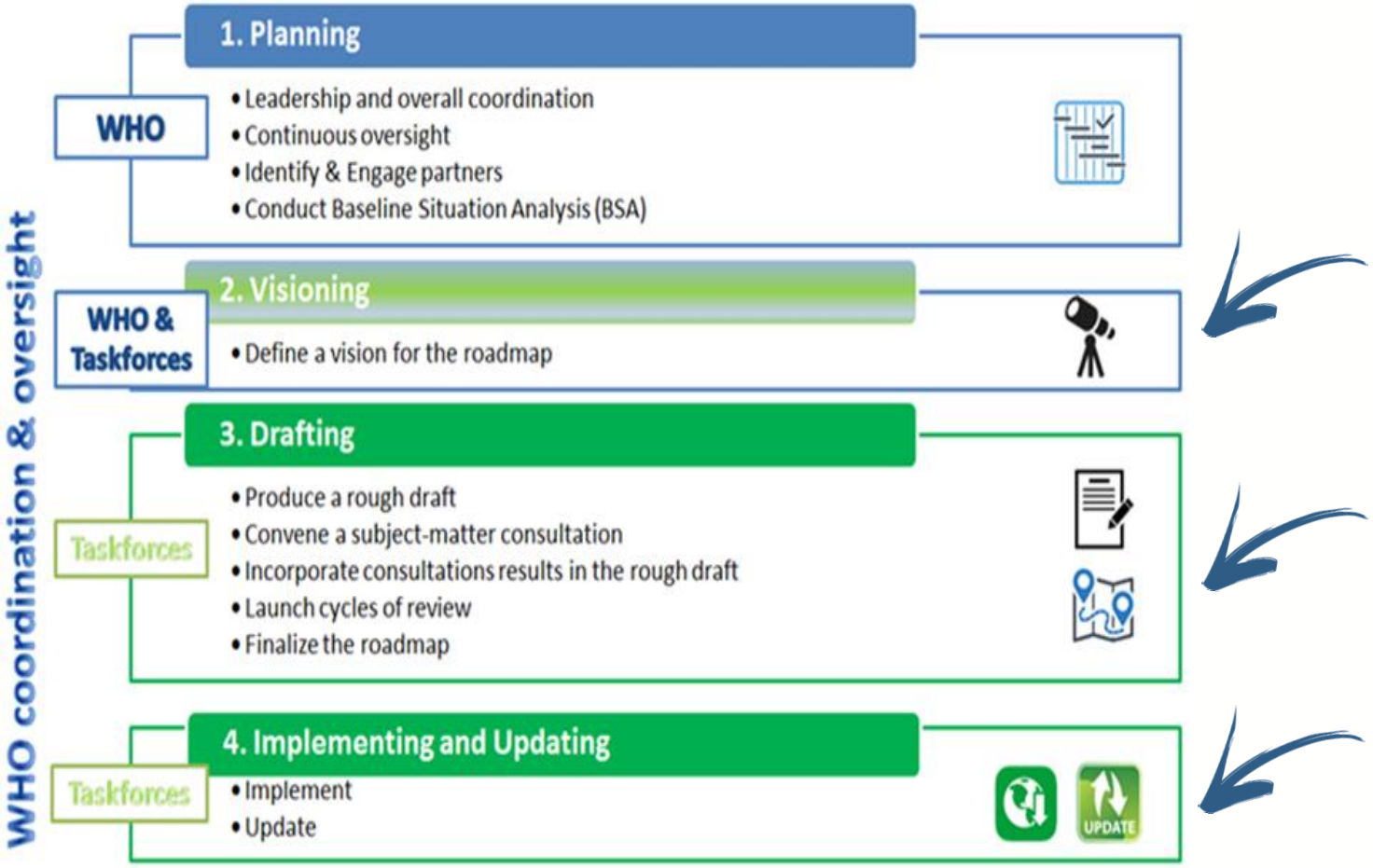
WHO to lead on a future Global Coordination Mechanism (GCM) for R&D preparedness and response - *Round Table, Chatham House 10 November 2016*

In terms of R&D Roadmaps, WHO will

- Lead, coordinate and ensure continuous oversight
- Establish and refine the **generic methodology**
- For each roadmap
  1. Baseline situation analysis (background paper)
  2. Identify and Engage Partners
  3. WHO target product profiles
- Develop and maintain a dashboard
- Ensure publication of roadmaps as joint products

# Context (cont'd)

As commissioned, **each roadmap taskforce** will be responsible for:



# A generic methodology

Developing and implementing R&D Roadmaps for priority pathogens with epidemic potential

R&D Blueprint roadmaps will form a strategic framework that underpins strategic goals and research priorities of the global R&D community

developed on the basis of

a **generic methodology**

purpose: to provide a standardized procedure that structures and harmonizes the development and implementation of R&D roadmaps

→ **First draft** circulated for internal review on 1 February 2017

**Presentation to SAG**

**Advanced draft** to be circulated to external selected experts for comments

→ **Working draft** by mid-March 2017

# A generic methodology

**Methodology Synopsis**

→ High level overview of principles and concepts, intended for peer-review publication

**Methodology**

**Core Document**

→Outline of the structure, design and implementation

**Appendices**

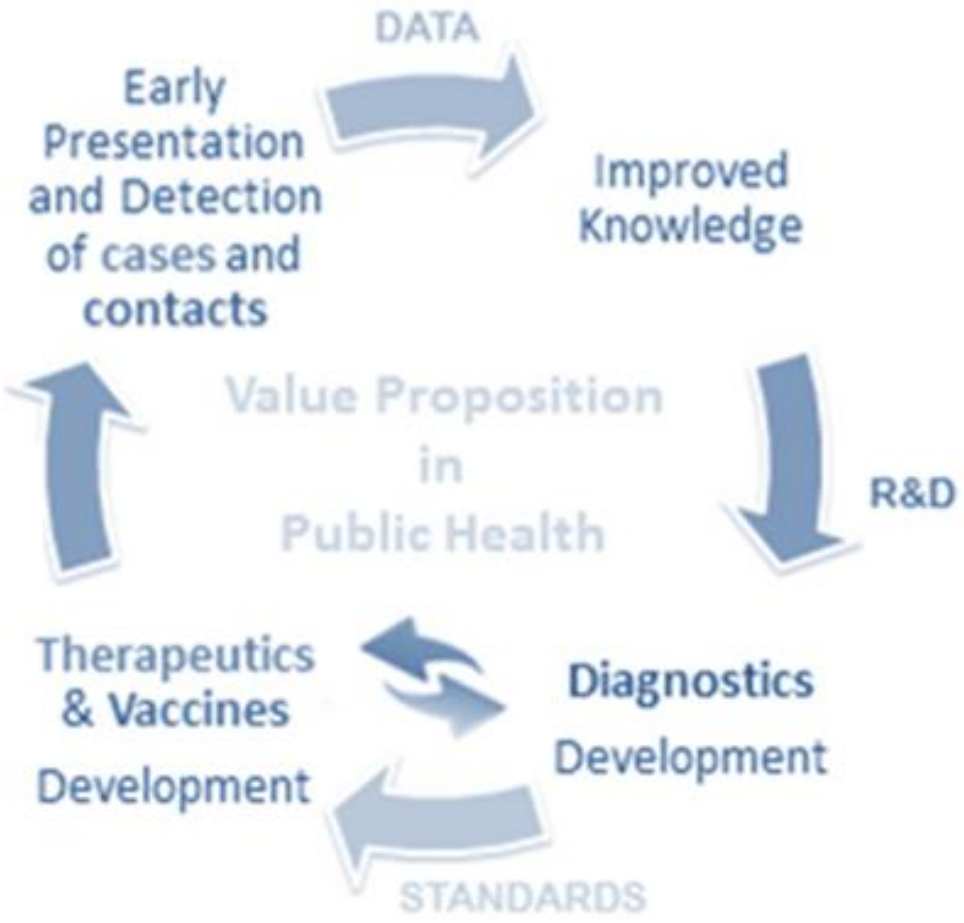
→Detailed instructions/steps for each of the roadmap elements

# Activities 2017

|  | Ebola - Marburg | CCHF | Zika | Lassa |
|---|---|---|---|---|
| **Consultant, collaborating centre (BSA)** | ✓ | ✓ | ✓ | ✓ |
| **Taskforce (roadmap)** | ongoing | ongoing | TBD | ongoing |
| **Roadmap expected** | End Q2 | End Q3 | End Q4 | End Q3 |
| **TPP** | Diagnostics<br>Ebola Vaccine<br>Multivalent-Filovirus-vaccine | TBD | Diagnostics<br>Vaccines | TBD |

✓ identified  ongoing  TBD to be done

# Discussion

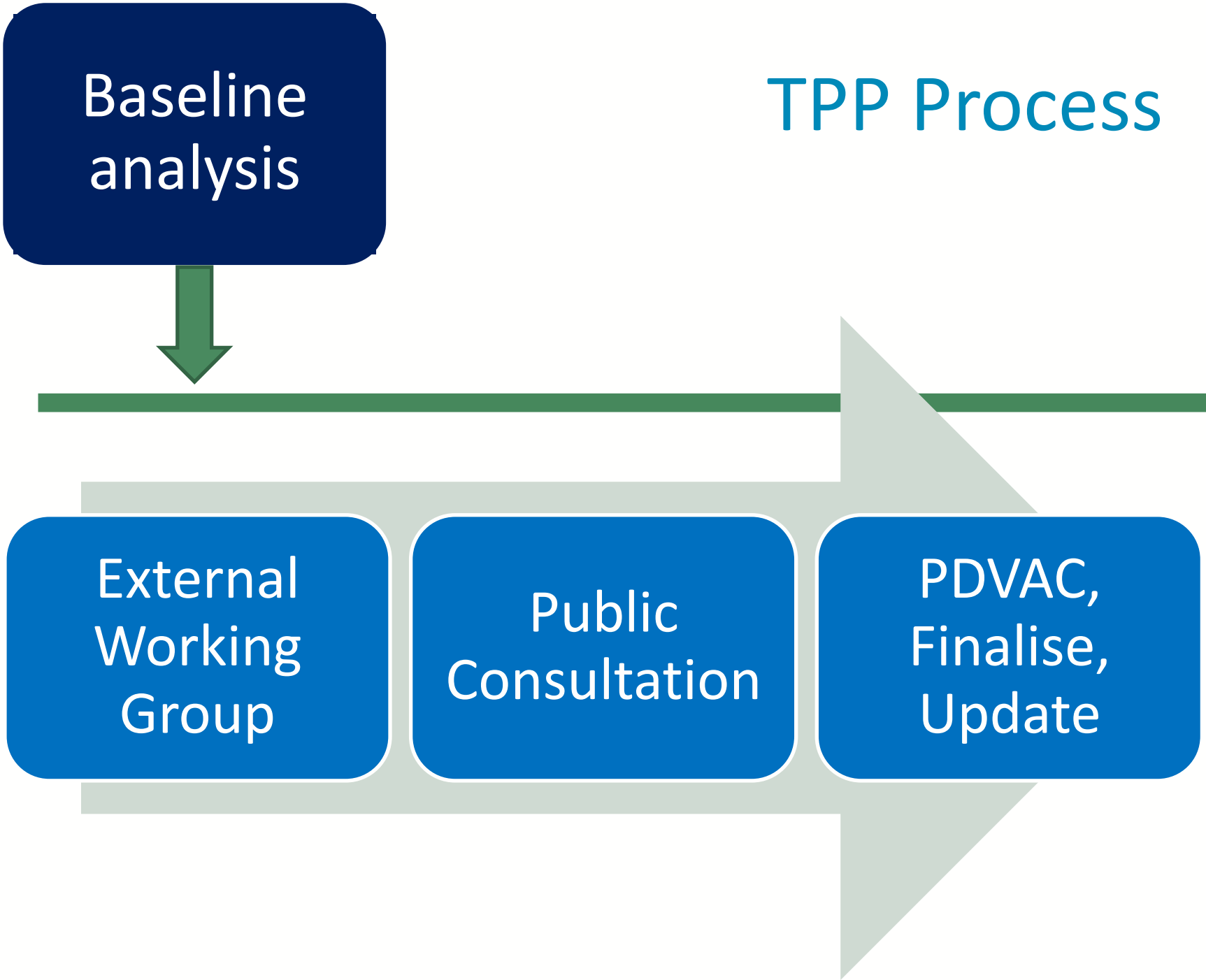

DATA
Early Presentation and Detection of cases and contacts
Improved Knowledge
Value Proposition in Public Health
R&D
Therapeutics & Vaccines Development
Diagnostics Development
STANDARDS

# What are the anticipated benefits?

The R&D roadmaps identify R&D gaps and help prioritize where investments should be channelled to initiate R&D initiatives; this will hopefully translate into interest from funders.

# Target Product Profiles

# TPP Process


Baseline analysis
External Working Group
Public Consultation
PDVAC, Finalise, Update

# MERS-CoV Vaccine TPPs

- Draft TPPs for 2 human vaccines and 1 camel vaccine open for public consultation

| Product | Phase | Country |
|---|---|---|
| **DNA vaccine** | **Phase 1 since 2016** | **USA** |
| **SAB Polyclonal** | **Phase 1 since 2016** | **USA** |
| MVA vaccine | Phase 1 Q1 2017 | Germany |
| ? Vaccine | Phase 1 2017 | South Korea |
| Chimp Ad vaccine | Phase 1 2017 | UK |
| Chimp Ad vaccine | In camel testing | Chad |

- Collaboration with OIE mobilizing animal vaccine stakeholders

# Development timeline for vaccine TPPs

| | Circulation of draft TPP to Expert Working group for comments | Public consultation of draft TPPs | Final TPP published at WHO website |
|---|---|---|---|
| Monovalent Ebola – reactive and preventive use | ✓ | ✓ | 2015 ✓ |
| Multivalent filovirus vaccine TPP – preventive use | ✓ | Oct 2016 ✓ | Nov 2016 ✓ |
| **Revised** Zika virus vaccine TPP **(first version, published July 2016)** | ✓ | Dec 2016 ✓ | Feb 2017 |
| MERS Co-V vaccine TPPs (3) | ✓ | Feb 2017 | March 2017 |
| Nipah Virus vaccine TPP | Q1 | Q1 | Q2 |
| Lassa Fever virus vaccine TPP | Q1 | Q2 | Q2 |

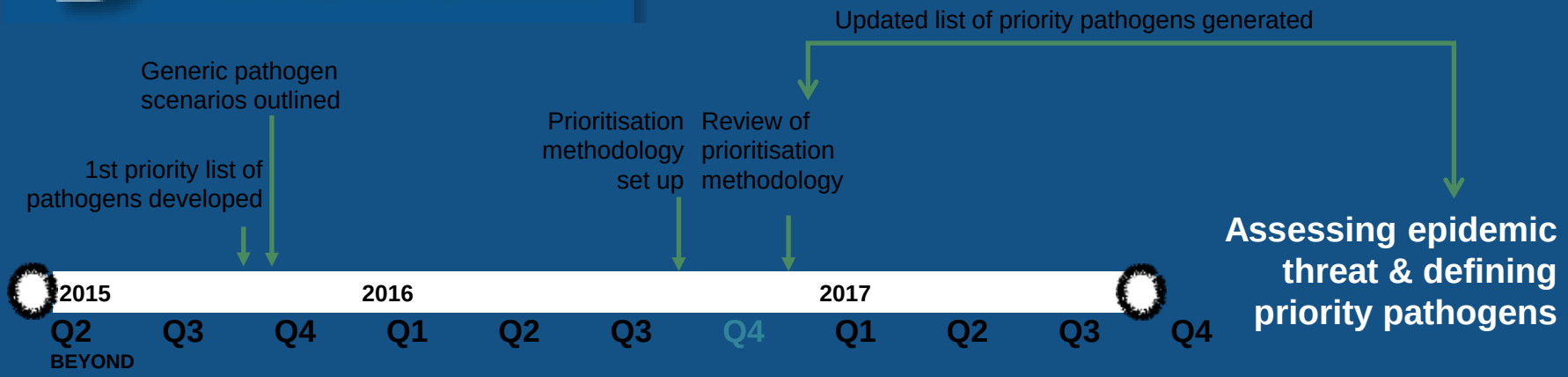
# Development timeline for diagnostic TPPs

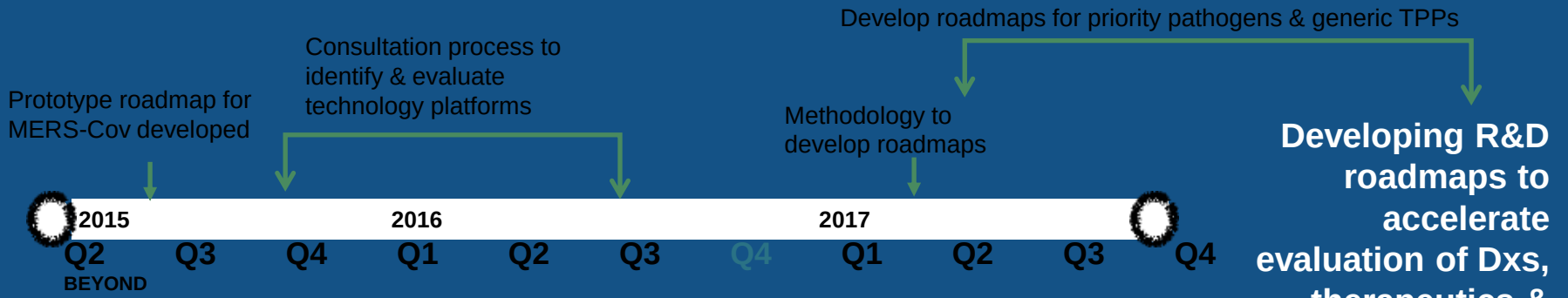
| | Circulation of draft TPP to Expert Working group for comments | Public consultation of draft TPPs | Final TPP published at WHO website |
|---|---|---|---|
| Zika virus diagnostics | March 2016 ✓ | April 2016 ✓ | April 2016 ✓ |
| **Revised** Ebola virus diagnostics **(first version, published Oct 2014)** | July 2017 | August 2017 | September 2017 |
| MERS CoV | | Q3 | Q4 |

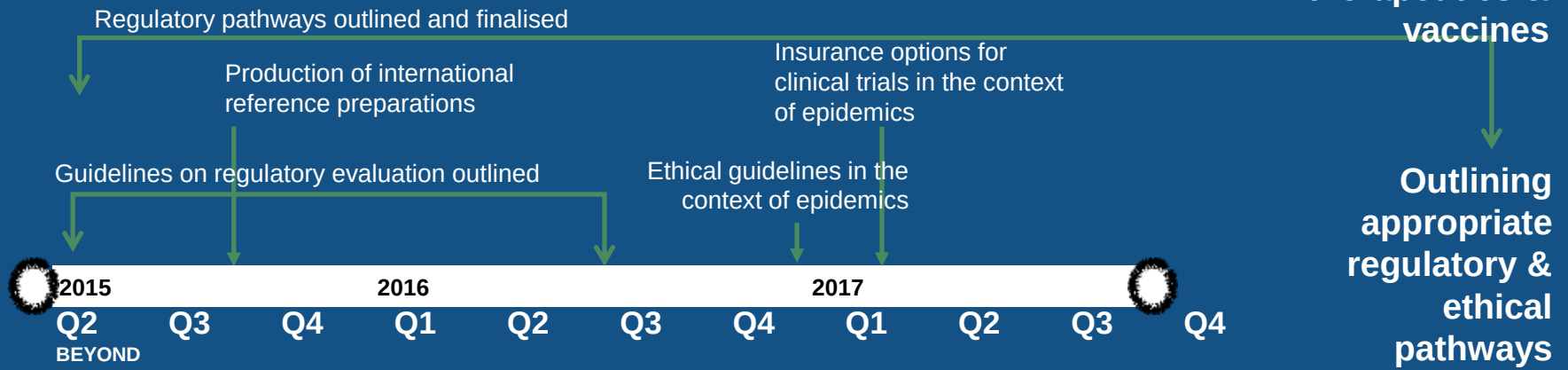
Also planned for 2017: MERS-CoV TPP including multivalent respiratory test for syndromic diagnosis of SARI (severe acute respiratory illness), approach to other syndromic diagnostics will be explored

# Regulatory Pathways

# B Accelerating Research & Development processes



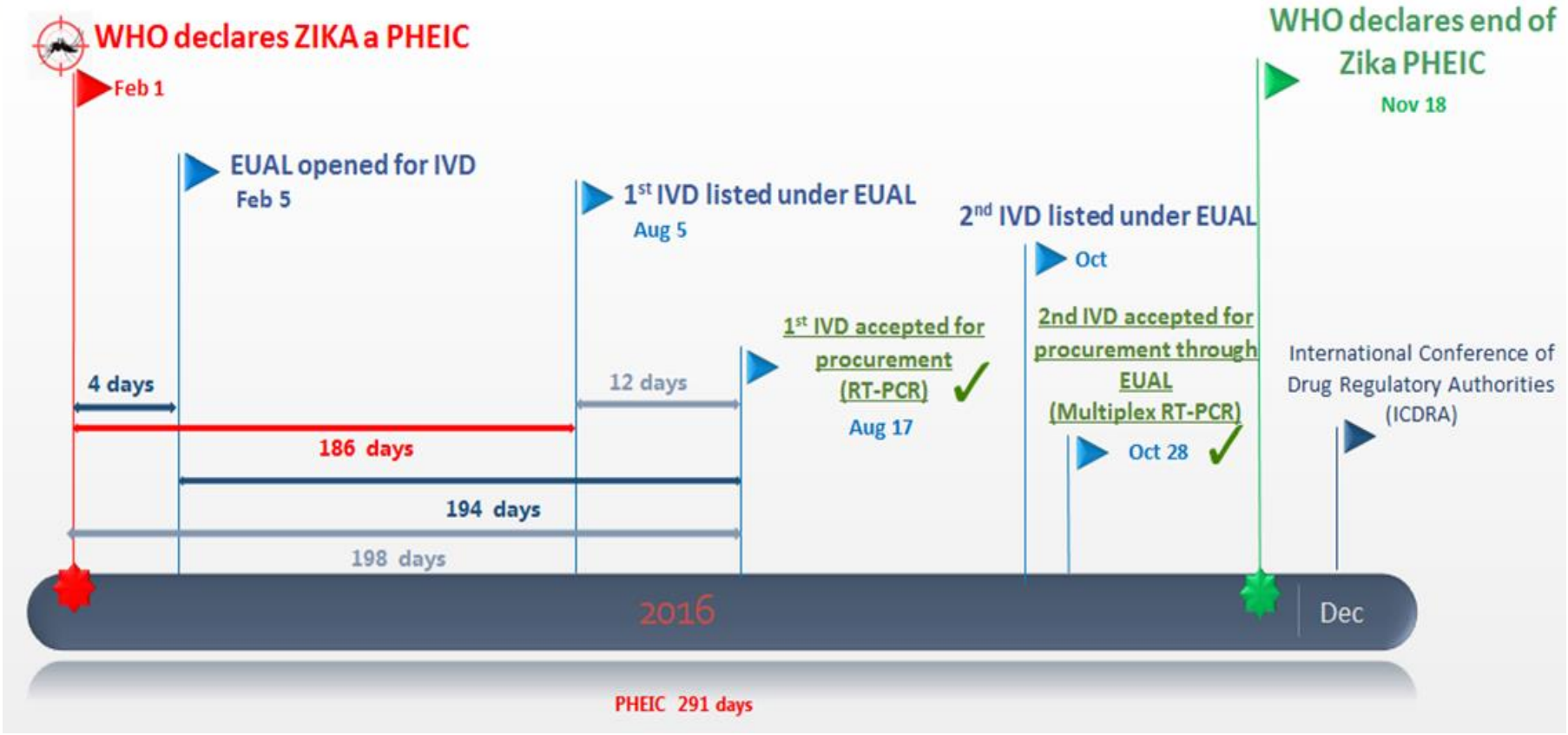



# Regulatory pathways

- Promoting **regulatory convergence** is recognized as a key enabler in the R&D Blueprint.

- WHO aims to assist efforts to accelerate research and development by
  - outlining appropriate regulatory & ethical pathways, and
  - by anticipating evidence needs to inform regulatory review

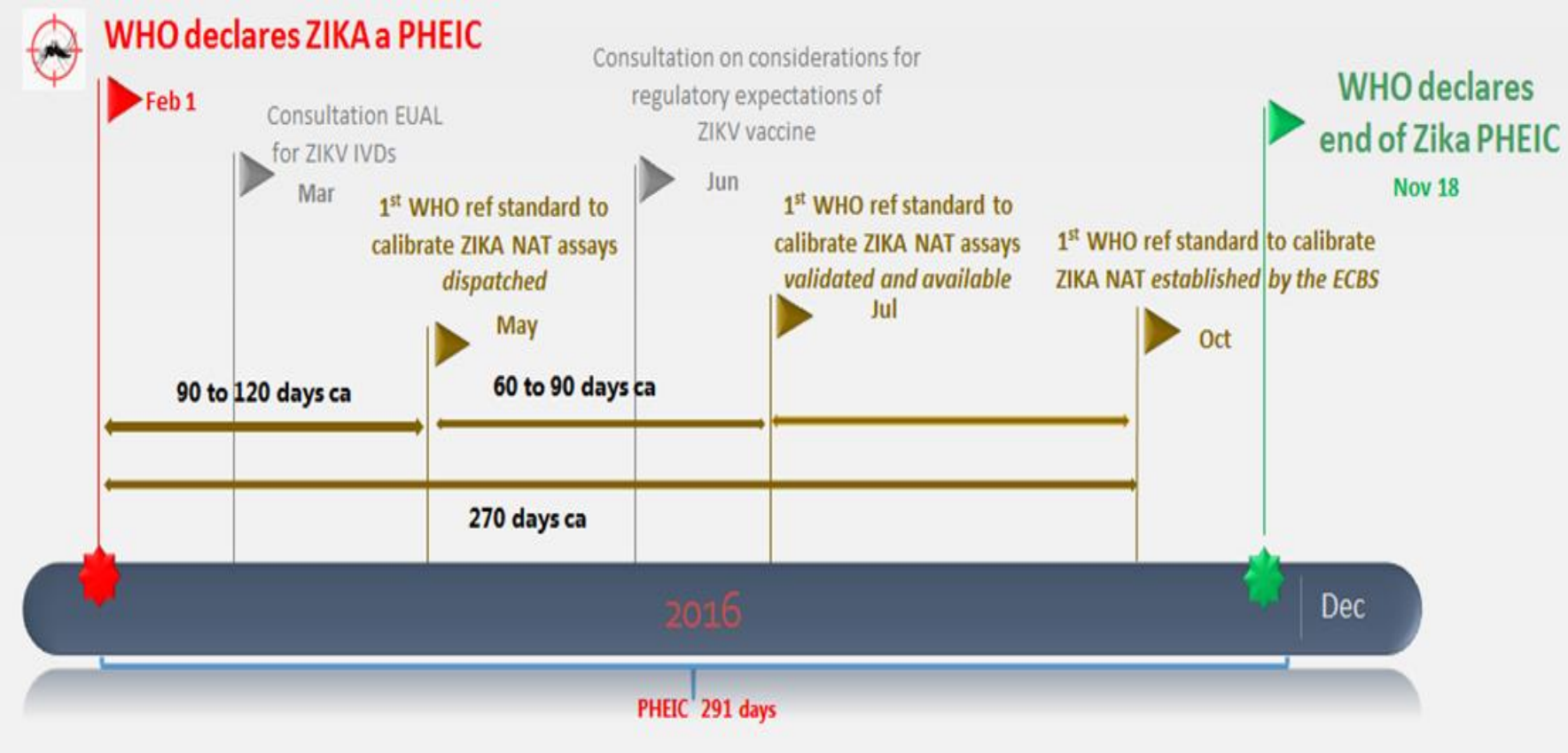
# EUAL listing of Zika IVDs




**As of January 18 2017, 15 applications submitted for ZIKA IVD EUAL remain under evaluation.**

Overall the submitted technical documentation has been poor, necessitating supplementary laboratory evaluation by WHO. Availability of laboratories to perform the evaluations has however been a constraint and efforts are ongoing to address the challenges.

# Validation and distribution of reference standards for Zika




The international collaborative study to validate the reference standard showed it was suitable for use to calibrate viral load assays in both blood and urine.

# Regulatory issues

## Identification and responding to regulatory gaps

International Conference of Drug Regulatory Authorities, Cape Town, December 2016
More than 360 regulators from more than 100 WHO Member States

**Gaps identified**

- **NRAs remain unprepared** to face a public health emergency
- **Lack of NRA capacity** in large parts of the developing world.
- Limited capacity and **experience in communicating with stakeholders**, particularly the media and public.
- Missed opportunity for **product developers to engage regulators early and often** in the process
- Problems with **access to data and samples**
- A poorly regulated environment -unscrupulous to take advantage through **fake products or dubious remedies**.

# Planned activities 2017: EUAL

- **Ad Hoc Committee for the Emergency Use of Vaccines** will be convened and advice on the suitability of Ebola vaccines for emergency use is anticipated in Q2 2017

- **Proactive identification of laboratories** capable of performing IVD evaluation studies on behalf of WHO for each of the priority pathogens will be completed by Q4 2017

- A consultation on **options for preparedness** to ensure access to products in future emergency settings, will be convened for vaccines, diagnostics and therapeutics against priority pathogens

# Planned activities: reference standards

- Completion of an **international collaborative study on reference preparations** to evaluate the suitability of a candidate WHO reference standard for Zika antibodies is anticipated in Q3 2017

- Work will start in 2017 in WHO Collaborating Centers to **develop candidate reference standards** for other priority pathogens (Ebola reference standards have already been established)

# Planned activities: regulatory guidelines

- Completion of **WHO guidelines on the regulatory evaluation of Ebola vaccines** is anticipated in Q3 2017

- A WHO consultation on **regulatory expectations for the evaluation of nucleic acid based vaccines** will be convened. This will consider the need to update existing guidance on DNA vaccines (WHO Technical Report Series 941) and expand the guidance to mRNA-based vaccines

- A WHO consultation is planned in Q3 2017 to estimate the **impact of emerging infections**, **including Zika, on the blood supply**, to facilitate regulatory decision making

# Planned activities: joint reviews

- **A joint review of clinical trial applications for lead candidate Zika vaccines** is being considered, contingent upon interest from the vaccine developers and requests from countries targeted for the forthcoming multi-country clinical trials

# What are the anticipated benefits?

A global regulatory resource is available to provide pro-active and convergent, but non-binding, advice concerning candidate products being developed against pathogens with the potential to cause public health emergencies of international concern.

Global regulatory capacity to respond to public health emergencies of international concern is increased, and readiness improved.

Issues of liability in case of mass vaccination with a product which has not yet been fully evaluated, do not slow down deployment of a needed vaccine.

# Developing new norms and standards adapted to the epidemic context

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

Tools: Methods design discussion, decision tree, annotated generic protocol

Steps outlined to develop tools to inform discussions on trial designs

Review of progress of 4 working parties

Draft tools available for vaccines

Initiate work for therapeutics

Wider consultation on tools for vaccines starts

**Supporting expansion of capacity to implement adequate study designs**

2015 2016 2017

Q2 BEYOND Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4

Review of general agreement forms & guidelines to support framing of collaborations

Biobanking platforms process initiated

Consultation on ownership, benefit sharing & IP

MTA capacity building tool

**Developing guidance & tools to frame collaborations and exchanges**

2015 2016 2017

Q2 BEYOND Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4

Develop global norms for sharing data & results during public health emergencies

SAGE recommendation on evidence need for policy making on Ebola vaccines

Consultation on data sharing

Consultation biobanking + decision tree data sharing WHO Statement Data sharing

**Anticipating evidence needs to inform regulatory review and policy development**

2015 2016 2017

Q2 BEYOND Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4

# Supporting expansion of capacity to implement adequate study designs

**March 2016**

30 leading experts met to discuss the rationale of designing a vaccine efficacy trial during public health emergencies and agreed on a collaborative research preparedness exercise .

The group includes experts in public health, vaccine trial methodologists, biostatisticians, infectious pathogen modelers, regulators, ethicists and funders.

**October 2016**

30 leading experts met to develop a plan on vaccines study methods to help decision making related to the clinical evaluation of vaccines for priority pathogens under the Blueprint.

# Supporting expansion of capacity to implement adequate study designs

Working groups are developing :

(i) a comprehensive **methodological discussion paper** on vaccine study designs;

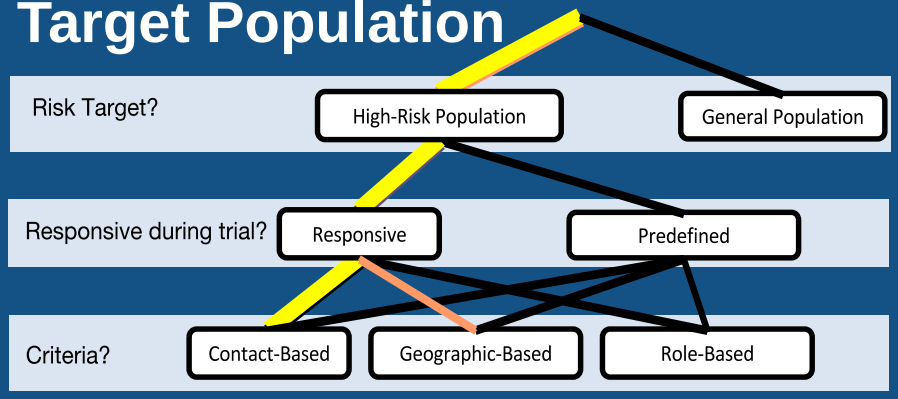
(ii) **a decision tree** to guide methodology experts during the design of a vaccine trial and promote discussion around key methodological choices;

(iii) **a trial simulator** using realistic outbreak scenarios to assess trials feasibility and;

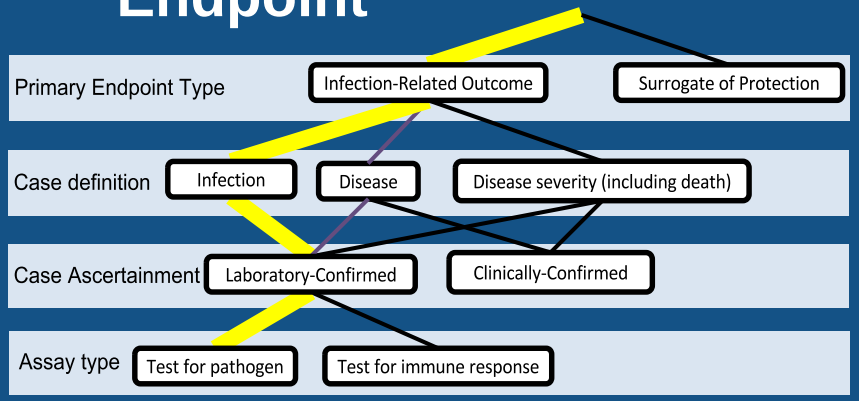
(iv) **generic annotated protocols** for various study designs.

# A decision tree to guide methodology experts during the design of a vaccine trial

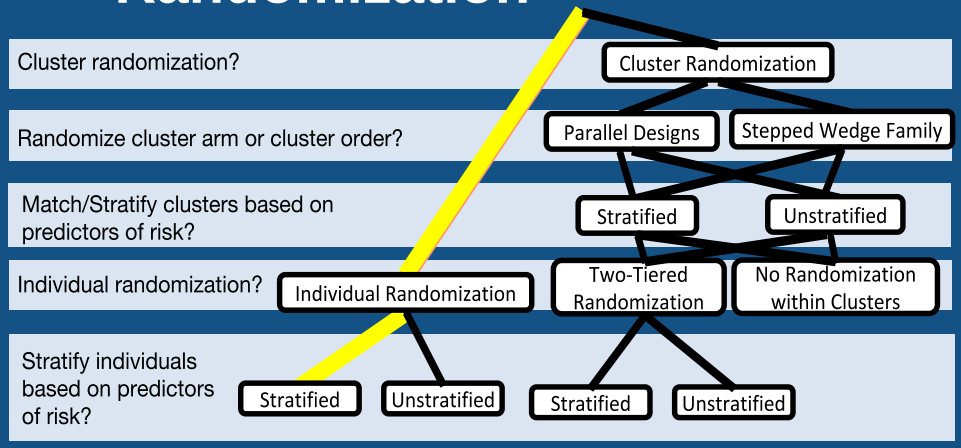
## Target Population



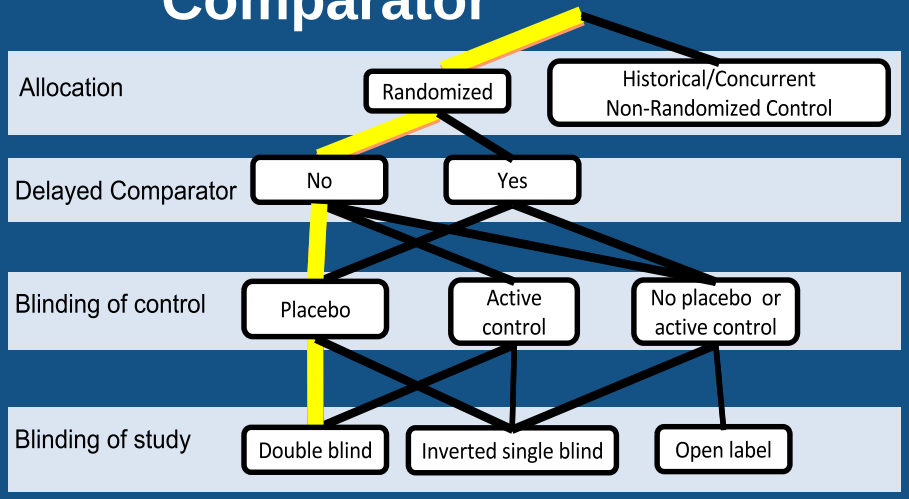

## Endpoint




## Randomization




## Comparator



# Supporting expansion of capacity to implement adequate study designs

**March 2017**
CREDO training workshop: to present scope of work.

**May 2017**
Work is underway with four expert groups. The progress will be presented and discussed. The tools are are expected in the third quarter of 2017.
Zika study designs workshops

**1st Quarter 2017**
A future phase of this work will focus on efficacy trial protocols for therapeutics.

# Anticipating evidence needs to inform regulatory review and policy development

## SAGE Working Group on Ebola vaccines and vaccination

http://www.who.int/wer/2015/wer9050.pdf

**2015**, **90**, 681-700 **No. 50**

World Health Organization

Organisation mondiale de la Santé

Weekly epidemiological record

Relevé épidémiologique hebdomadaire

11 DECEMBER 2015, 90th YEAR / 11 DÉCEMBRE 2015, 90e ANNÉE

**No. 50**, **2015**, **90**, 681–700

http://www.who.int/wer

**Contents**



**Sommaire**



### Meeting of the Strategic Advisory Group of Experts on immunization, October 2015 – conclusions and recommendations

The Strategic Advisory Group of Experts on immunization (SAGE)[1] met on 20–22 October 2015. This report summarizes the discussions, conclusions and recommendations.[2] For the malaria session, SAGE was joined by the Malaria Policy Advisory Committee (MPAC) and the conclusions and recommendations concerning malaria vaccine are those of both committees.

### Réunion du Groupe stratégique consultatif d'experts sur la vaccination, octobre 2015 – conclusions et recommandations

Le Groupe stratégique consultatif d'experts sur la vaccination (SAGE)[1] s'est réuni du 20 au 22 octobre 2015. Le présent rapport résume les discussions, conclusions et recommandations auxquelles il est parvenu.[2] Le Comité de pilotage de la politique de lutte antipaludique (MPAC) s'est joint au SAGE pour la session consacrée au paludisme: les conclusions et recommandations relatives au vaccin antipaludique émanent donc de ces deux Comités.

# Anticipating evidence needs to inform regulatory review and policy development

**March 2017**

SAGE Working Group on Ebola Vaccines

To review updated evidence on immunogenicity, efficacy, effectiveness and safety of candidate Ebola vaccines and, on the observed and projected impact of different vaccination strategies using compassionate use data and from mathematical models.

**April 2017**

SAGE session for DECISION on Ebola Vaccines

Previous SAGE recommendations http://www.who.int/wer/2015/wer9022.pdf?ua=1

# SAGE Working Group on Ebola Vaccines

**To consider the following questions that will be presented for SAGE's consideration in 2017:**

- Are there remaining challenges that may prevent access to Ebola vaccines in future outbreaks, and if yes can SAGE make recommendations on how these might be addressed?
- Is the current evidence sufficient for SAGE to make recommendations regarding the use Ebola vaccines (e.g. rVSV and the Russian vaccine) in case of another Ebola outbreak (pre-licensure and/or post licensure)?
  - If yes, which recommendations can be proposed?
  - If not, what key data are missing?

# What are the anticipated benefits?

Clinical trial designs for testing efficacy of vaccines and therapies against priority pathogens are discussed and agreed before an outbreak. This allows quick implementation in case of need, country ownership and fosters partners' coordination.

# Material Transfer Agreements

## Development of a capacity building tool

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

Tools: Methods design discussion, decision tree, annotated generic protocol

Steps outlined to develop tools to inform discussions on trial designs

Review of progress of 4 working parties

Draft tools available for vaccines

Initiate work for therapeutics

Wider consultation on tools for vaccines starts

**Supporting expansion of capacity to implement adequate study designs**

2015 2016 2017

Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4

BEYOND

Review of general agreement forms & guidelines to support framing of collaborations

Biobanking platforms process initiated

Consultation on ownership, benefit sharing & IP

MTA capacity building tool

**Developing guidance & tools to frame collaborations and exchanges**

2015 2016 2017

Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4

BEYOND

Develop global norms for sharing data & results during public health emergencies

SAGE recommendation on evidence need for policy making on Ebola vaccines

Consultation on data sharing

Consultation biobanking + decision tree data sharing

WHO Statement Data sharing

**Anticipating evidence needs to inform regulatory review and policy development**

2015 2016 2017

Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4

BEYOND

# Consultation on an MTA guidance tool

## 16 December 2016. Paris, France

- Held in collaboration with Institute Pasteur
- Focused on public health emergencies
- Convened diverse stakeholder communities to:
  - Lessons from recent PHEICs
  - Cross-cutting issues
  - Contents of MTAs – inc. ownership, benefit sharing & IP
- Did **not** attempt to resolve differences of opinion or develop a single model
- Did further efforts to map different approaches & options

# Consolidating diverse discussions

## Past meetings

- May 2015 – WHO 1st Consultation on Biobanking
- August 2015 – WHO 2nd Consultation on Biobanking
- September 2015 – WHO consultation on data sharing
- January 2016 – Wellcome Trust meeting on biobanking tools
- April 2016 – WHO policy statement on data sharing
- May 2016 – Wellcome Trust meeting on IP, benefit sharing & public health emergencies

# Consolidating diverse discussions

## Other processes and projects

- **Chatham House** project to build tools to strengthen sharing of routine public health surveillance data
- **Duke University** mapping of legal texts under the Global Healthcare Innovation Alliances
- **OpenMTA** developed by the Biobricks Foundation & Open Plant Initiative
- MTAs developed and used in an African context by **Uganda National Council for Science &Technology**
- **MSF** efforts to prepare for future health emergencies

# Overview of an MTA tool

## Scope & contents

Informal consultation noted tool will need to provide:

- An introductory overview of MTAs
- A guide to overarching principles
- Further detail of what is expected in an MTA
- Guidance on how agreements in different areas of an MTA relate to one another.
- The different possible approaches, and how to go about constructing them
- Case studies.

# Next steps & future work

- Develop a draft MTA tool based on existing material (2017 Q1)
- Expand the stakeholders involved through an online public consultation (2017 Q1)
- Revise draft contents & feed into WHO 3rd Biobanking consultation (2017 Q2)
- Test material with possible users (inc. relevant ministries and end users) (2017 Q2-3 onwards)
- Develop digital tool & make available in public beta test (2017 Q3 onwards)

# What are the anticipated benefits?

Guidance and tools enable barriers to data and sample sharing to be incrementally addressed, so that timelines are accelerated in future outbreaks. This allows control measures to be better implemented, available interventions to be more effectively deployed, and experimental interventions to be evaluated efficiently.

# Developing guidance and tools for collaborations and exchanges

## Data and sample sharing

R&D BLUEPRINT

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

Tools: Methods design discussion, decision tree, annotated generic protocol

Steps outlined to develop tools to inform discussions on trial designs

Review of progress of 4 working parties

Draft tools available for vaccines

Initiate work for therapeutics

Wider consultation on tools for vaccines starts

**Supporting expansion of capacity to implement adequate study designs**

2015 2016 2017

Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4

BEYOND

Review of general agreement forms & guidelines to support framing of collaborations

Biobanking platforms process initiated

Consultation on ownership, benefit sharing & IP

MTA capacity building tool

**Developing guidance & tools to frame collaborations and exchanges**

2015 2016 2017

Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4

BEYOND

Develop global norms for sharing data & results during public health emergencies

SAGE recommendation on evidence need for policy making on Ebola vaccines

Consultation on data sharing

Consultation biobanking + decision tree data sharing

WHO Statement Data sharing

**Anticipating evidence needs to inform regulatory review and policy development**

2015 2016 2017

Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4

BEYOND

# Data Sharing: Consensus on the need for change

World Health Organization

centre | Publications | Countries | Programmes | Governance | About WHO

Essential medicines and health products

## Developing global norms for sharing data and results during public health emergencies

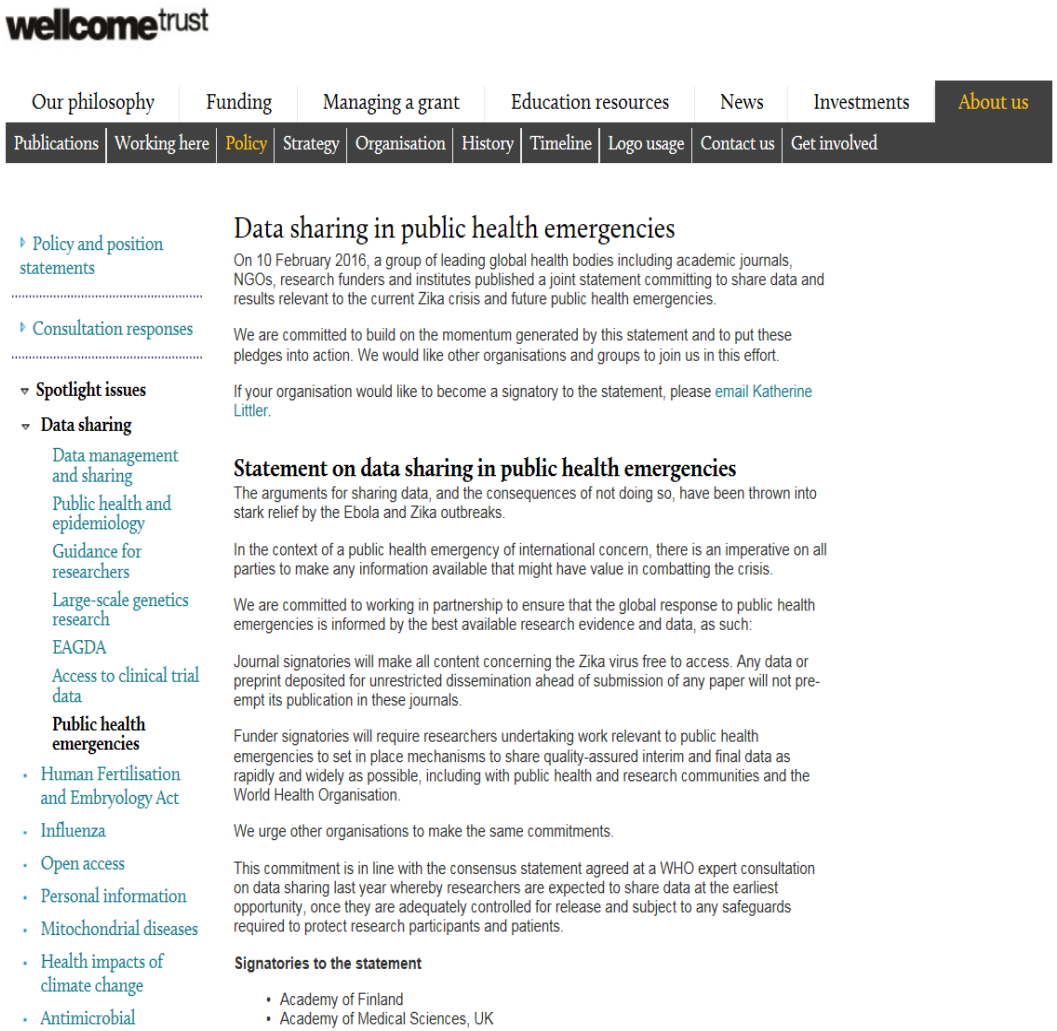
Statement arising from a WHO Consultation held on 1-2 September 2015

Leading international stakeholders from multiple sectors convened at a WHO consultation in September 2015, where they affirmed that timely and transparent pre-publication sharing of data and results during public health emergencies must become the global norm.

The following summary points represent WHO's position with regard to data and results sharing in public health emergencies, having taken into account the perspectives of those who attended the meeting.

### Summary Points

1. Research is essential in the context of public health emergencies. The primary purpose of such research is to advance public health, prevent illness and save lives. Researchers should always weigh the public health consequences of their actions in withholding and sharing results.



wellcome trust

Our philosophy | Funding | Managing a grant | Education resources | News | Investments | About us

Publications | Working here | Policy | Strategy | Organisation | History | Timeline | Logo usage | Contact us | Get involved

- Policy and position statements
- Consultation responses
- Spotlight issues
- Data sharing
  - Data management and sharing
  - Public health and epidemiology
  - Guidance for researchers
  - Large-scale genetics research
  - EAGDA
  - Access to clinical trial data
  - **Public health emergencies**
- Human Fertilisation and Embryology Act
- Influenza
- Open access
- Personal information
- Mitochondrial diseases
- Health impacts of climate change
- Antimicrobial

## Data sharing in public health emergencies

On 10 February 2016, a group of leading global health bodies including academic journals, NGOs, research funders and institutes published a joint statement committing to share data and results relevant to the current Zika crisis and future public health emergencies.

We are committed to build on the momentum generated by this statement and to put these pledges into action. We would like other organisations and groups to join us in this effort.

If your organisation would like to become a signatory to the statement, please email Katherine Littler.

### Statement on data sharing in public health emergencies

The arguments for sharing data, and the consequences of not doing so, have been thrown into stark relief by the Ebola and Zika outbreaks.

In the context of a public health emergency of international concern, there is an imperative on all parties to make any information available that might have value in combatting the crisis.

We are committed to working in partnership to ensure that the global response to public health emergencies is informed by the best available research evidence and data, as such:

Journal signatories will make all content concerning the Zika virus free to access. Any data or preprint deposited for unrestricted dissemination ahead of submission of any paper will not pre-empt its publication in these journals.

Funder signatories will require researchers undertaking work relevant to public health emergencies to set in place mechanisms to share quality-assured interim and final data as rapidly and widely as possible, including with public health and research communities and the World Health Organisation.

We urge other organisations to make the same commitments.

This commitment is in line with the consensus statement agreed at a WHO expert consultation on data sharing last year whereby researchers are expected to share data at the earliest opportunity, once they are adequately controlled for release and subject to any safeguards required to protect research participants and patients.

**Signatories to the statement**

- Academy of Finland
- Academy of Medical Sciences, UK

# Research data sharing in outbreaks/PHE

Sep 2015 R&D Blueprint consultation has been taken up and “ownership” is felt by several groups as a consensus statement.

Wellcome Trust has been identified as lead party under Global Coordination Mechanism. WHO works to support Wellcome in this role.

Some progress in articulation of enabling policies:

# Research data sharing in outbreaks/PHE

Some progress in articulation of enabling policies:

- Operationalising WHO policy statement on data sharing in the context of PHE through developing data sharing frameworks for different categories of stakeholders with different types of data
- *Genetic sequence data*: Code of conduct for rapid sharing of pathogen genome sequencing in outbreaks
- *Medical Journals:* Working with ICMJE on enabling policy for pre-publication information sharing (eg Zika open)
- *Multiple audiences (funders, researchers, member states*): Guidance on data sharing agreements between 3rd parties
- *R&D Funders*: Engaging with GLOPID-R network of funders on data sharing policies

# Challenges to overcome

Developing an effective system of incentives for data sharing

Agreeing norms, principles and developing capacities for 3rd party data sharing platforms

Mainstreaming pre-publication platforms (eg BioRxiv, F1000Research)

Ethical issues – 2 related WHO guidance documents (surveillance, outbreaks)

Legal issues – guidance on data sharing agreements

Capacity development in low income settings

# WHO Guidance for managing ethical issues in infectious pathogen outbreaks - 2016


http://apps.who.int/iris/bitstream/10665/250580/1/9789241549837-eng.pdf.

# Linking with other key initiatives – Chatham House Public Health Surveillance Data Sharing Initiative

## Strengthening Data Sharing for Public Health

This project aims to develop guidelines on how to create the right environment for public health data sharing and achieve good practice. The project will take these recommendations to key stakeholders within global health to provide support for pushing the established norms for data sharing towards a model where data are shared as openly as is possible and appropriate.

CHATHAM HOUSE
The Royal Institute of International Affairs

# Compliance with registration and reporting of clinical trials

Operationalizing WHO policy based on position statement from 2015

- Universal prospective registration in WHO ICTRP compliant registry
- Public disclosure of summary results within 12 months of study completion (shorter timelines during ongoing emergency!)

**Developing WHO action plan/checklist for actions for different stakeholders**

**Global Clinical Trials activity to go live in WHO R&D Observatory later this month**

**Looking for resources to provide ongoing tracking of trials reporting to WHO ICTRP database**

# Conclusion

Multiple areas of incremental but not game-changing progress

Some progress in articulation of enabling policies

Still issues in implementation

Trust will be paramount

# What are the anticipated benefits?

Guidance and tools enable barriers to data and sample sharing to be incrementally addressed, so that timelines are accelerated in future outbreaks. This allows control measures to be better implemented, available interventions to be more effectively deployed, and experimental interventions to be evaluated efficiently.

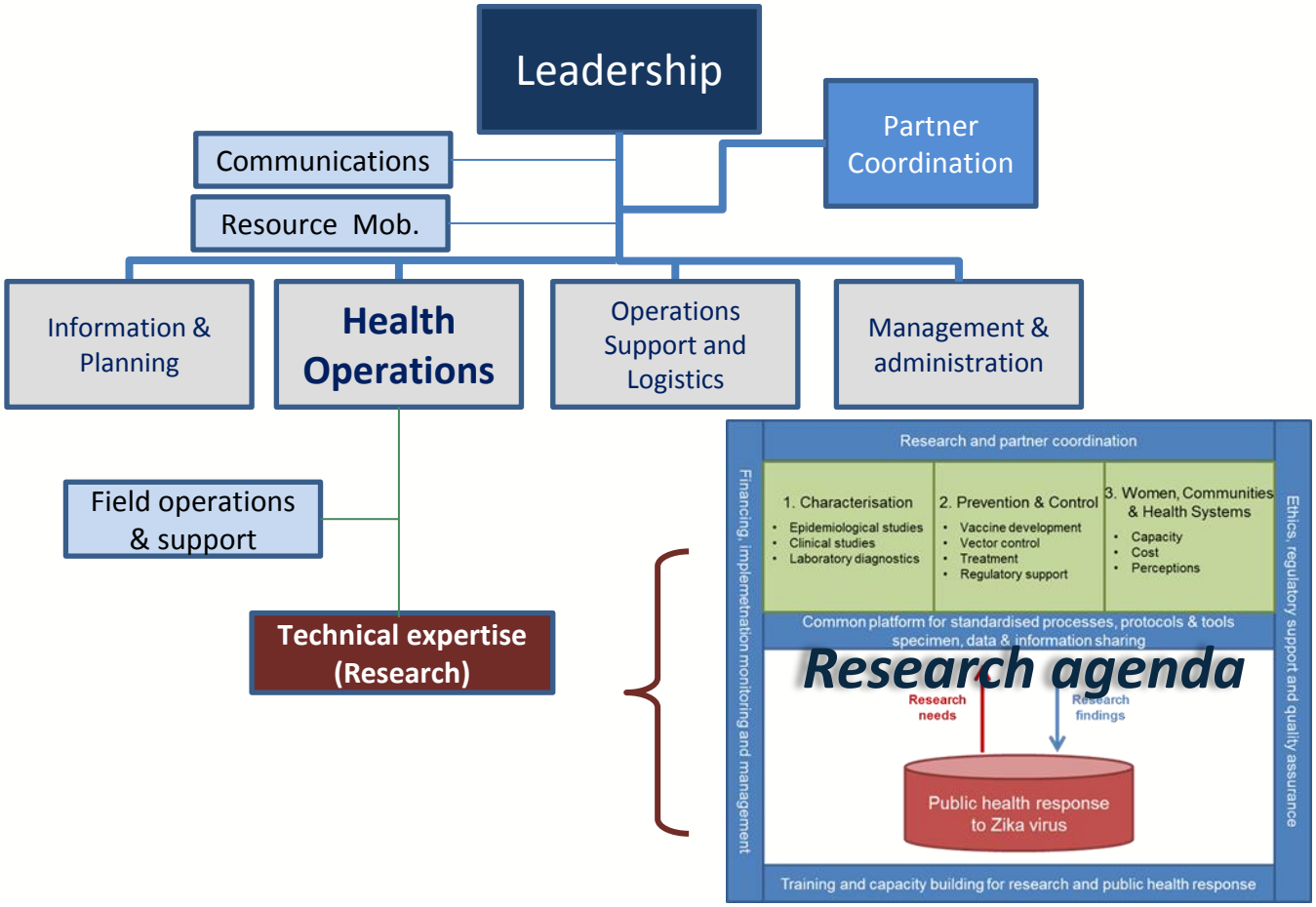
# R&D response to outbreaks

## Streamlined operational R&D response during outbreaks

R&D
BLUEPRINT

# Response to Zika

## WHO Incident Management Structure




**3 WHO clusters (OHE; FWC; HIS), and PAHO**

# Blueprint Zika R&D activities

- Landscape analysis of products
- Diagnostic TPP to detect active infection/prior infection
- Emergency Use Assessment & listing (EUAL) procedure
- Reference reagents
- Vaccine TPP to protect against Congenital Zika Syndrome for use during an emergency
- WHO Vaccine Pipeline Tracker

# Blueprint ZIKA R&D meetings

- WHO global consultation of research related to Zika virus infection.

  7-9 March 2016; Geneva

- WHO consultation for the EUAL procedure for Diagnostics.

  14-15 March 2016; Geneva

- WHO consultation on considerations for regulatory expectations of Zika virus vaccines for use during an emergency.

  6-7 June 2016; Geneva

- A common approach to tackling mosquito-borne viruses to pre-empt epidemics.

  WHO-Wellcome Trust, 5-7 October 2016; London

- Scientific Consultation on ZIKV vaccine.

  NIAID-WHO, 10-11 January 2017; Washington

# ZIKA: Post emergency plan

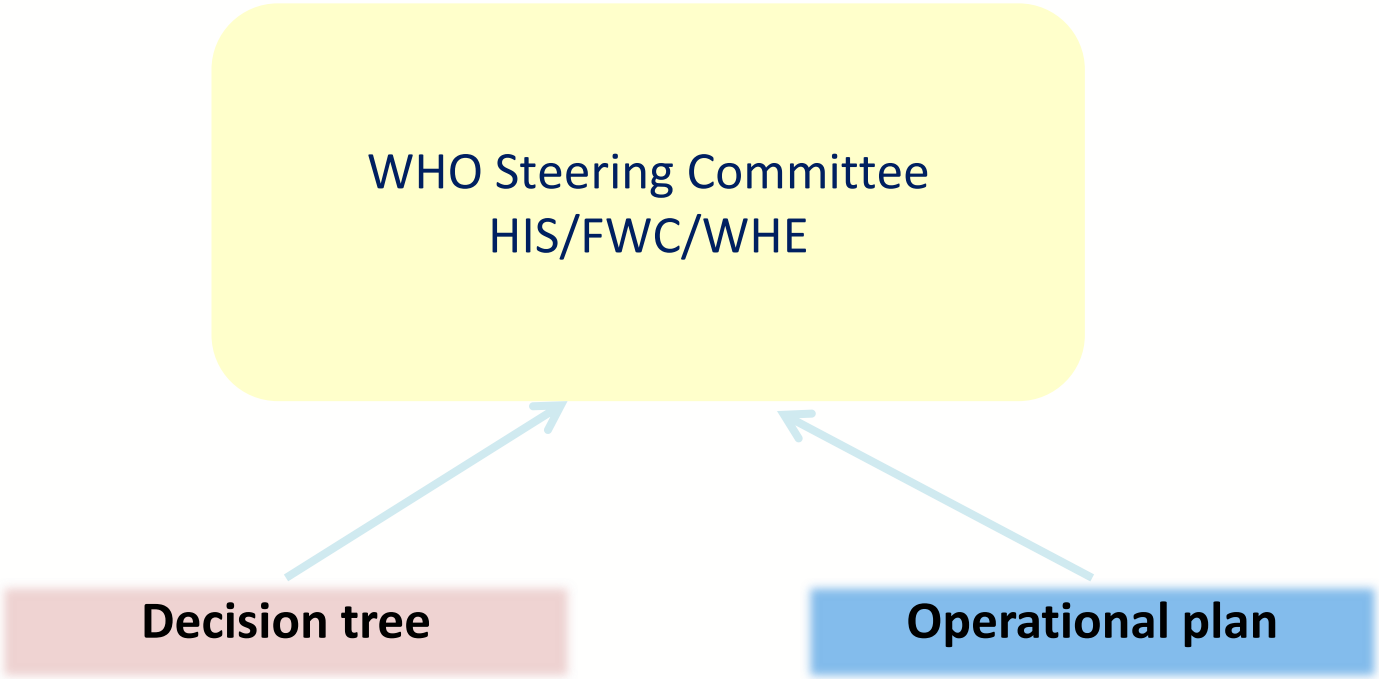
## Emergency Committee 18 November 2016

- **Zika virus and associated consequences remain a significant enduring public health challenge requiring intense action but no longer represent a PHEIC as defined under the IHR**
- **Robust longer-term technical mechanism is now required to manage the global Zika response**

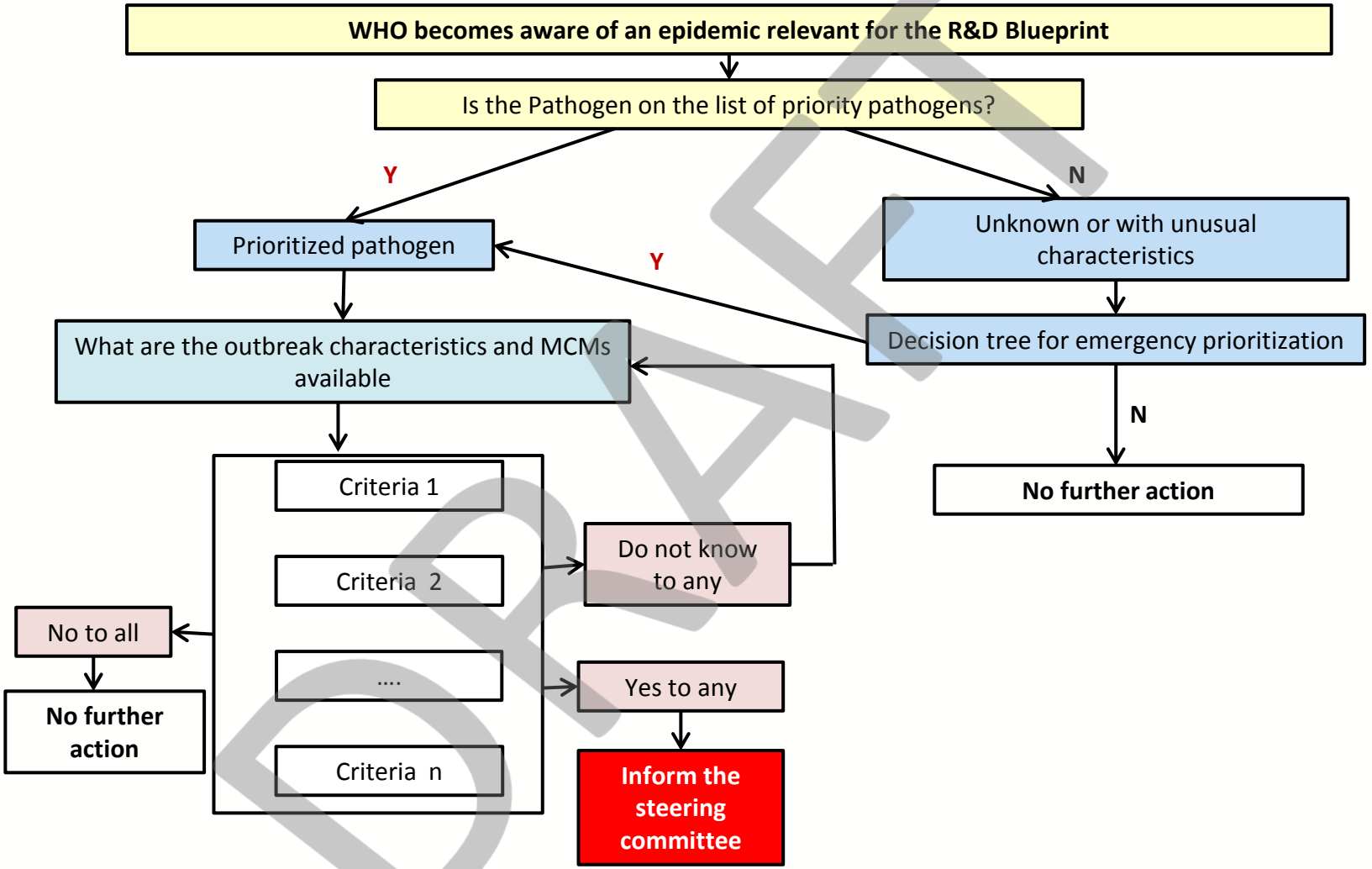
## Transition plan towards a long-term programme

# R&D response mechanisms

***Internal WHO coordination and planning***



# Decision tree



# Operational plans

Three outbreak scenarios

- Priority pathogens with no MCMs available,
- Priority pathogens with some MCMs available
- Outbreaks caused by an unknown pathogen

Detailed operational plans for:

- Staffing and budget needs
- Reallocation of staff
- Additional resource needs

WHO Global (product and non-product) Research Agenda

# Blueprint R&D response to an epidemic