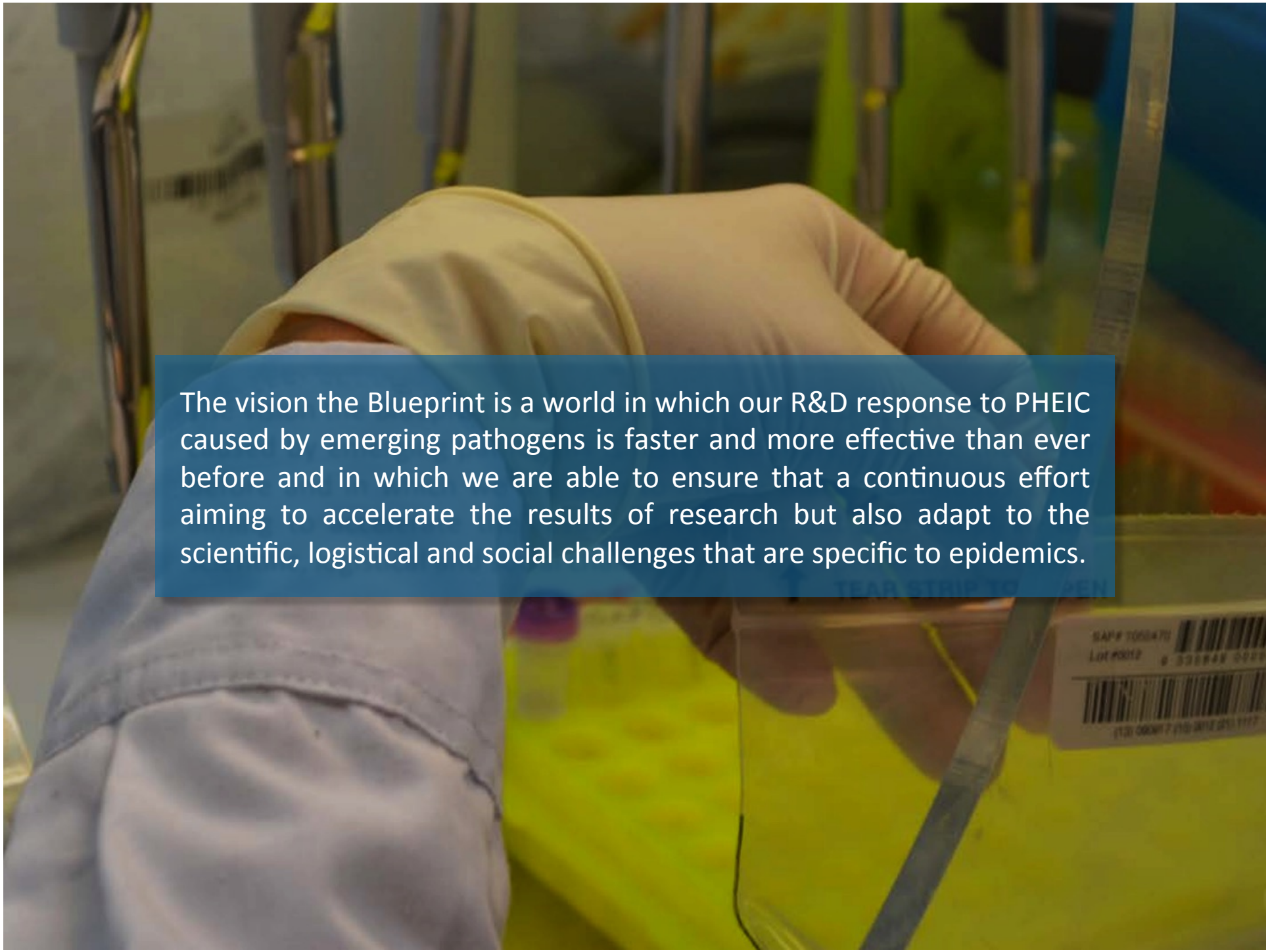
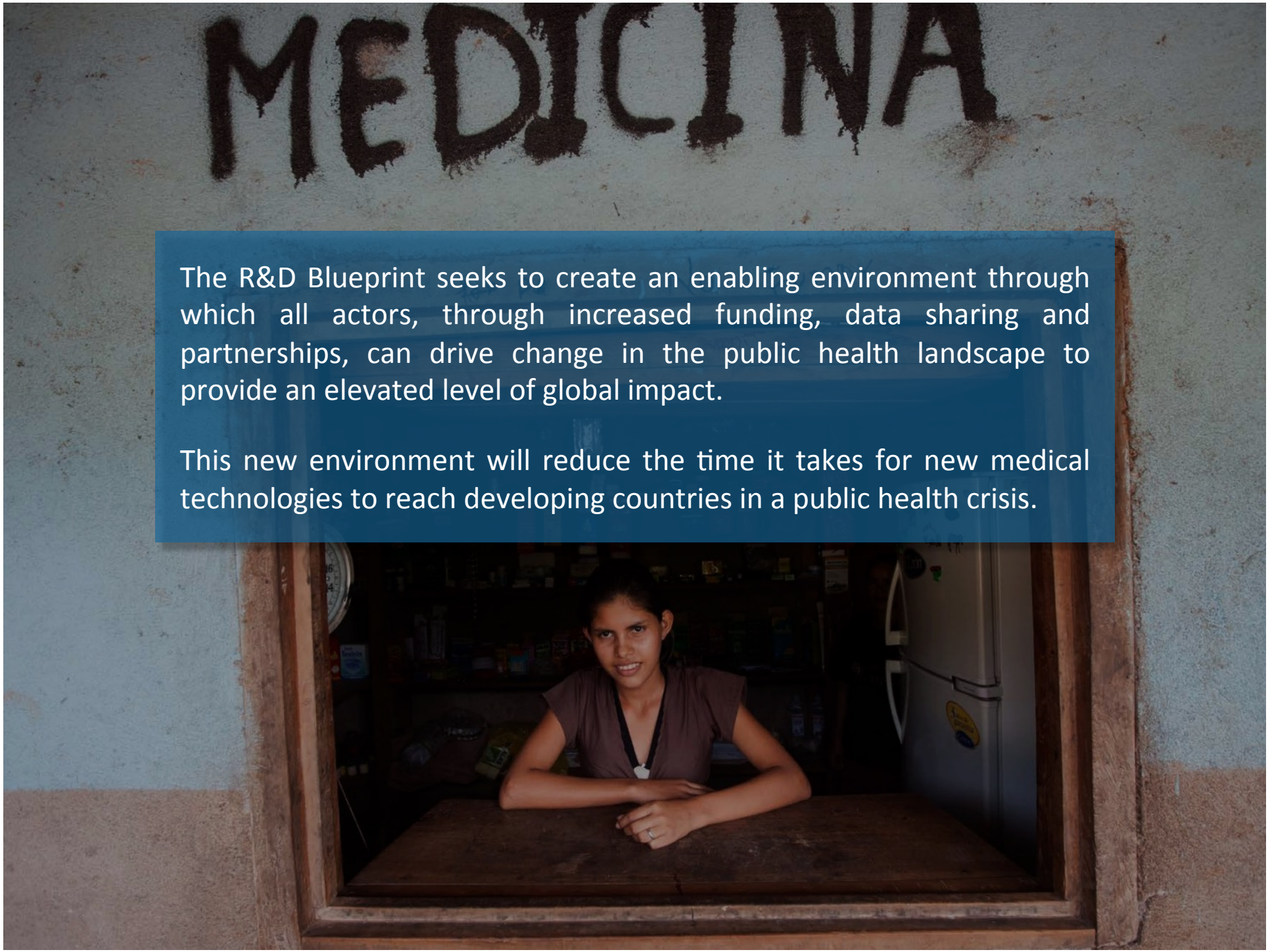
WHO R&D Blueprint

Processes and methods for prioritization of diseases


The vision the Blueprint is a world in which our R&D response to PHEIC caused by emerging pathogens is faster and more effective than ever before and in which we are able to ensure that a continuous effort aiming to accelerate the results of research but also adapt to the scientific, logistical and social challenges that are specific to epidemics.

In May 2015, the Sixty-Eighth World Health Assembly:

...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 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.

This new environment will reduce the time it takes for new medical technologies to reach developing countries in a public health crisis.

Core approaches

A Improving coordination & fostering an enabling environment

B Accelerating Research & Development processes

C Developing new norms and standards adapted to the epidemic context

a. Assessing epidemic threat & defining priority pathogens

b. Developing R&D roadmaps to accelerate evaluation of diagnostics, therapeutics & vaccines

c. Outlining appropriate regulatory & ethical pathways

Priority diseases

There's an urgent need for R&D for:

- Arenaviral hemorrhagic fevers (including Lassa Fever)
- Crimean Congo Haemorrhagic Fever (CCHF)
- Filoviral diseases (including Ebola and Marburg)
- Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
- Other highly pathogenic coronaviral diseases (such as Severe Acute Respiratory Syndrome, (SARS))
- Nipah and related henipaviral diseases
- Rift Valley Fever (RVF)
- Severe Fever with Thrombocytopenia Syndrome (SFTS)
- Zika

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

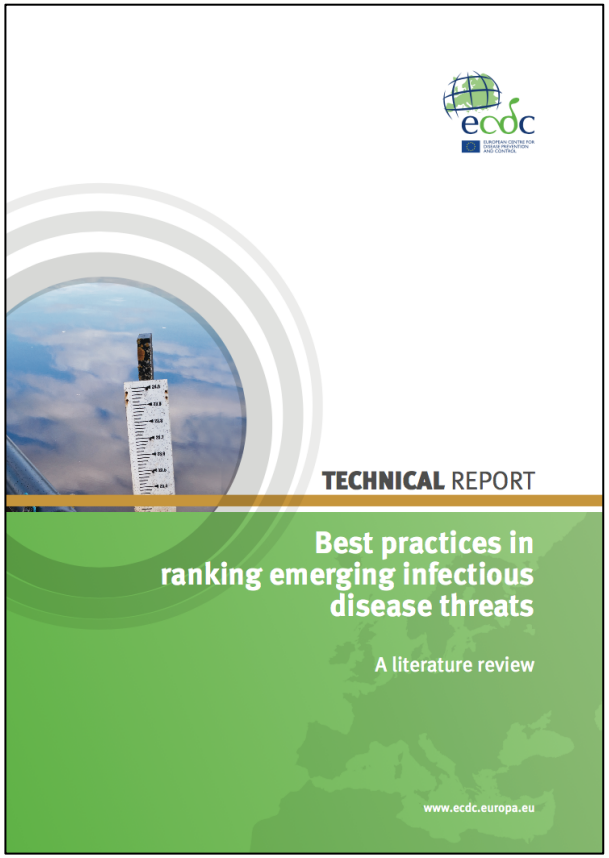
Other areas of substantial output

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

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

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

A robust methodology was needed



Reporting lacked detail... Unclear how criteria were developed… Potential sources of bias and mitigations are not reported. The publication was not peer-reviewed and it is unclear if any other review took place… Delphi scoring was limited to one round. Did not meet all of the key communicable disease facets. 95% confidence intervals used to aid discussion of discrepancies in scoring

Timeline

Activities undertaken to-date

May 2015 – WHO international consultation on Blueprint

December 2015 – WHO informal consultation on priority diseases

Early 2016 – Blueprint team develops methodology outline

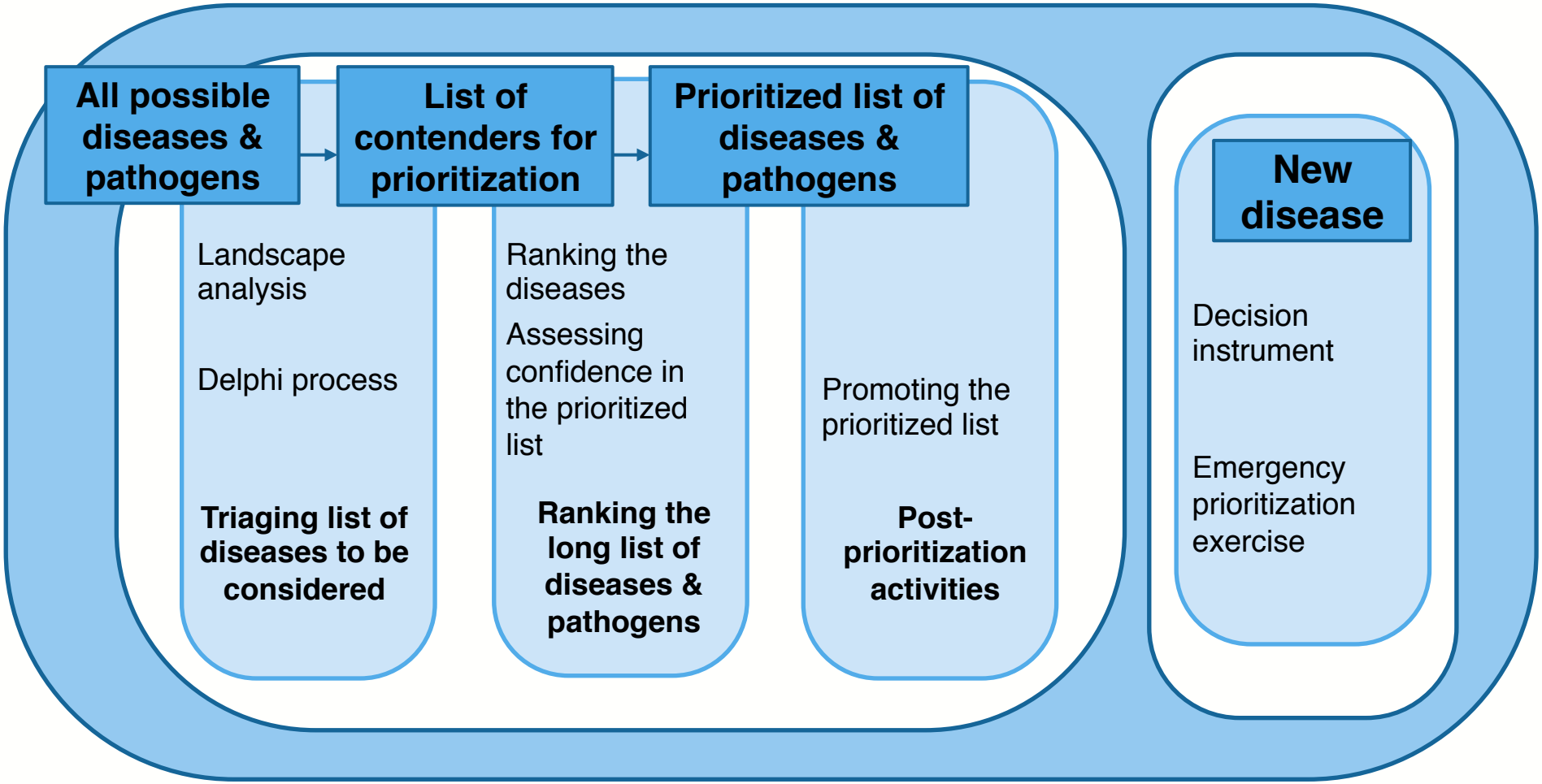
May 2016 – SAG reviews methodology outline

Summer / Autumn 2016 – Detailed methodology developed

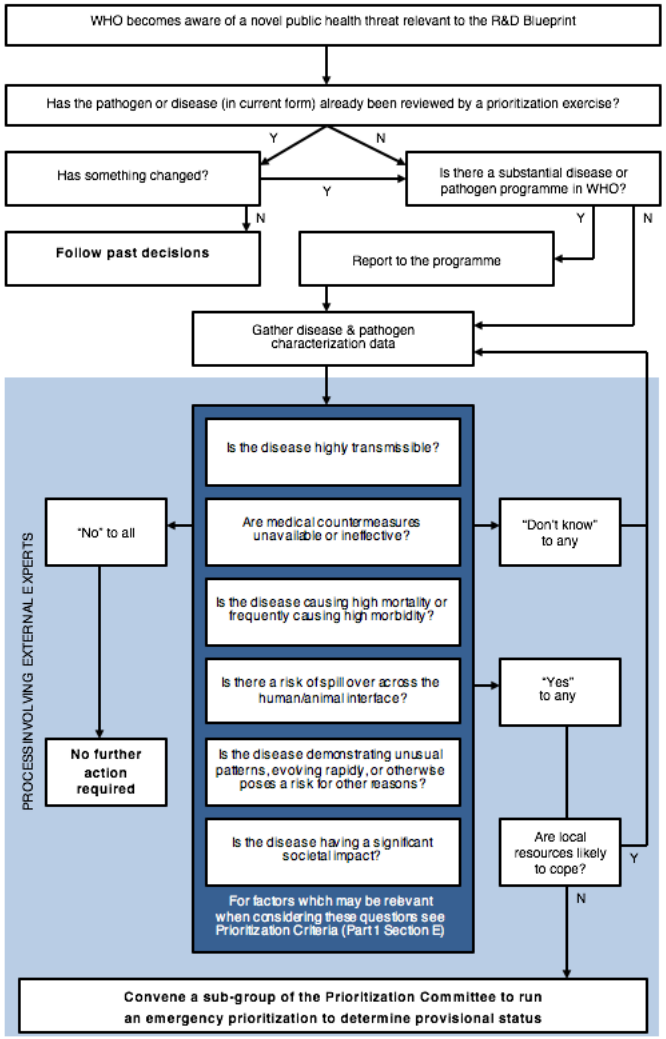
December 2016 – Informal consultation reviews & validates methodology

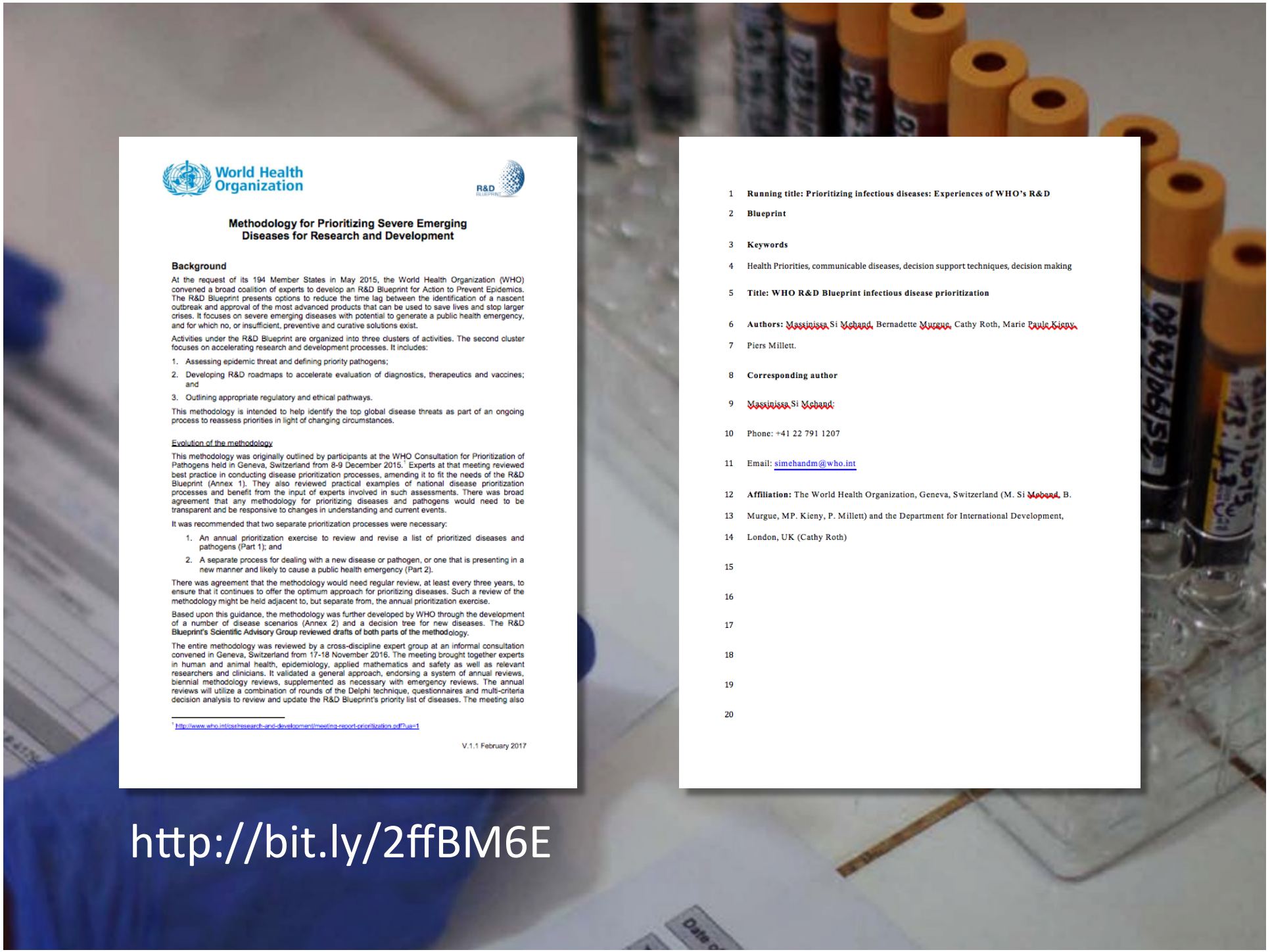
January 2017 – Annual review of list of priority diseases

Overview of the prioritization process



Decision instrument for new diseases





World Health Organization

R&D BLUEPRINT

Methodology for Prioritizing Severe Emerging Diseases for Research and Development

Background

At the request of its 194 Member States in May 2015, the World Health Organization (WHO) convened a broad coalition of experts to develop an R&D Blueprint for Action to Prevent Epidemics. The R&D Blueprint presents options to reduce the time lag between the identification of a nascent outbreak and approval of the most advanced products that can be used to save lives and stop larger crises. It focuses on severe emerging diseases with potential to generate a public health emergency, and for which no, or insufficient, preventive and curative solutions exist.

Activities under the R&D Blueprint are organized into three clusters of activities. The second cluster focuses on accelerating research and development processes. It includes:

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

This methodology is intended to help identify the top global disease threats as part of an ongoing process to reassess priorities in light of changing circumstances.

Evolution of the methodology

This methodology was originally outlined by participants at the WHO Consultation for Prioritization of Pathogens held in Geneva, Switzerland from 8-9 December 2015.[1] Experts at that meeting reviewed best practice in conducting disease prioritization processes, amending it to fit the needs of the R&D Blueprint (Annex 1). They also reviewed practical examples of national disease prioritization processes and benefit from the input of experts involved in such assessments. There was broad agreement that any methodology for prioritizing diseases and pathogens would need to be transparent and be responsive to changes in understanding and current events.

It was recommended that two separate prioritization processes were necessary:

1. An annual prioritization exercise to review and revise a list of prioritized diseases and pathogens (Part 1); and
2. A separate process for dealing with a new disease or pathogen, or one that is presenting in a new manner and likely to cause a public health emergency (Part 2).

There was agreement that the methodology would need regular review, at least every three years, to ensure that it continues to offer the optimum approach for prioritizing diseases. Such a review of the methodology might be held adjacent to, but separate from, the annual prioritization exercise.

Based upon this guidance, the methodology was further developed by WHO through the development of a number of disease scenarios (Annex 2) and a decision tree for new diseases. The R&D Blueprint's Scientific Advisory Group reviewed drafts of both parts of the methodology.

The entire methodology was reviewed by a cross-discipline expert group at an informal consultation convened in Geneva, Switzerland from 17-18 November 2016. The meeting brought together experts in human and animal health, epidemiology, applied mathematics and safety as well as relevant researchers and clinicians. It validated a general approach, endorsing a system of annual reviews, biennial methodology reviews, supplemented as necessary with emergency reviews. The annual reviews will utilize a combination of rounds of the Delphi technique, questionnaires and multi-criteria decision analysis to review and update the R&D Blueprint's priority list of diseases. The meeting also

[1] http://www.who.int/csr/research-and-development/meeting-report-prioritization.pdf?ua=1

1 **Running title: Prioritizing infectious diseases: Experiences of WHO's R&D**
2 **Blueprint**

3 **Keywords**

4 Health Priorities, communicable diseases, decision support techniques, decision making

5 **Title: WHO R&D Blueprint infectious disease prioritization**

6 **Authors:** Massinissa Si Mehand, Bernadette Murgue, Cathy Roth, Marie Paule Kieny,
7 Piers Millett.

8 **Corresponding author**

9 Massinissa Si Mehand:

10 Phone: +41 22 791 1207

11 Email: simehandm@who.int

12 **Affiliation:** The World Health Organization, Geneva, Switzerland (M. Si Mehand, B.
13 Murgue, MP. Kieny, P. Millett) and the Department for International Development,
14 London, UK (Cathy Roth)

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Prioritization criteria

Factors used to prioritize diseases

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%

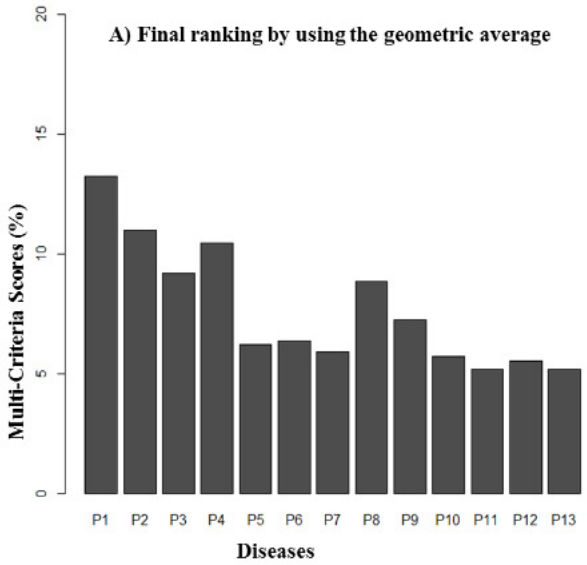
Prioritization Committee

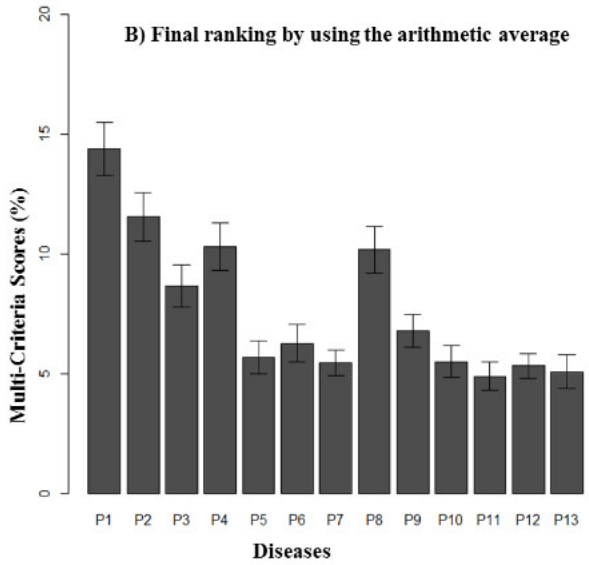
Regionally & gender diverse experts in:

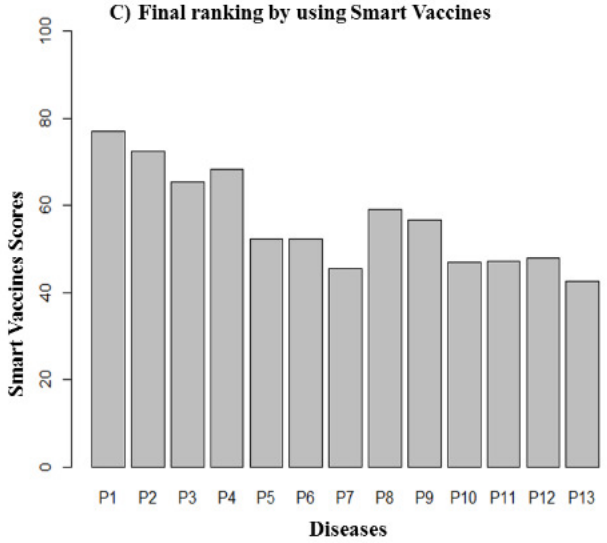
- Microbiology of severe pathogens
- Clinical management of severe infections
- Epidemiology
- Public health policy
- Animal health
- Anthropology
- Bioethics
- Biological weapons

Relative scoring

Indicative results







Confidence indicators

- Other studies
- Discordance intervals
- Multi-scenario sensitivity analysis
  - Removal of weightings
  - Suppression of highly weighted criteria
  - Changing weight of criteria (All +20% & +50%)
- Repetition with another scoring tool

Conclusions

- WHO developed its own methodology to prioritize diseases of relevance to Blueprint
- Built upon best practice
- Corrects earlier methodological shortcomings
- Balances need for repeatable methodology with expert input
- Fully publicly available
- Process to update methodology (next update 2018)
- Robust confidence in results produced