The WHO Global Observatory on Health Research and Development (R&D)

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Coordinator, Research, Ethics, Knowledge Uptake Health Systems and Innovation Cluster

World Health Organization
Funding stakeholders

- R&D Blueprint
- AMR R&D priorities
- PDVAC/Vaccines
- STI R&D priorities
- HTM, NTD, TDR priorities

Adaptable to regional and country health research monitoring and planning
What is the Global Observatory on Health R&D?

- The Global Observatory on Health R&D (‘the Observatory’) is a **centralized and comprehensive source of information** and **analyses** on global health R&D activities for human diseases.

- Observatory aim: to **map and synthesis** health R&D activities to enable evidence-based decisions on **R&D priorities by** the newly established **WHO Expert Committee on health R&D**.

- **Target users**: Governments, policy-makers, funders, researchers.

- **URL**: [www.who.int/research-observatory/en/](http://www.who.int/research-observatory/en/)
Background

- World Health Assembly mandated the establishment of the Observatory in resolution WHA66.22.

- **May 2016: WHA69.23** WHA requested the establishment of an expert committee on health R&D to set priorities for new investments based on information primarily provided by the Observatory.

- R&D Observatory / Expert Committee to include focus on AMR R&D and R&D Blueprint on emerging infectious diseases
  
  - **May 2014, WHA67.25**
  
  - WHO Executive Board, EB138/28
Scope

• Primary scope (as outlined in World Health Assembly resolution WHA69.23):

  – antimicrobial resistance and emerging infectious diseases likely to cause major epidemics.

  – potential areas where market failure exist;

  – type II and type III diseases (i.e. diseases incident in both rich and poor countries, but with a substantial proportion of the cases in poor countries, and diseases that are overwhelmingly or exclusively incident in developing countries respectively);

  – the specific R&D needs of developing countries in relation to type I diseases (i.e. diseases incident in both rich and poor countries, with large numbers of vulnerable populations in each);

• As more data and resources become available, the Observatory will expand the diseases and types of health research it covers.
How is it being developed?

- The Observatory:
  - builds on existing data and reports from a wide range of data sources
  - gathers new information (where needed and feasible).

- The WHO Secretariat:
  - works with its technical departments and their established expert groups and committees in order to develop and/or review analyses and syntheses produced by the Observatory;
  - seeks regular feedback on the Observatory’s structure and outputs from potential users including national policy-makers, academia, WHO’s technical experts and other international governmental organizations and global partnerships, WHO regional offices, civil society and industry stakeholders.
Collaborations

Fostering collaborations

12 currently in R&D Observatory; with *expanding coverage*

Expansions

Exploring new areas

work on R&D data classification & standards; inclusion of product profile directory; World RePORT
What is covered?

• Content is organized in six sections:

  - Monitoring inputs, processes and outputs
  - Benchmarking
  - R&D indicators
  - Analyses and syntheses
  - Databases and resources
  - Classifications and standards
Monitoring funding: exploring the data

- Information is visualized using Tableau™ software.
- Users can select and deselect items to customize data output according to their interest.
- For instance, for Malaria, users will see that the bulk of R&D investments from 2007-2015 (nearly US$ 5.1 billion) went into R&D for medicines, vaccines and basic research (US$ 4.6 billion). Only US$ 0.3 billion of investments went into vector control R&D.
Health Products in Pipeline

Across 23 mostly neglected diseases: 352 products are captured between various phases of developments as of May 2017.

### Number of products by type

<table>
<thead>
<tr>
<th>Product type</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccines</td>
<td>136</td>
</tr>
<tr>
<td>Medicines</td>
<td>109</td>
</tr>
<tr>
<td>Diagnostics</td>
<td>66</td>
</tr>
<tr>
<td>Vector cont.</td>
<td>38</td>
</tr>
<tr>
<td>Biologics</td>
<td>3</td>
</tr>
<tr>
<td>Blood produc.</td>
<td>1</td>
</tr>
</tbody>
</table>

### Number of products by phase

<table>
<thead>
<tr>
<th>R&amp;D phase</th>
<th>Evaluation</th>
<th>Clinical</th>
<th>Licensed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I</td>
<td>37</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>Phase II</td>
<td>83</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>Phase III</td>
<td>47</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Clinical (unspecified)</td>
<td>30</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Licensed / Phase IV</td>
<td>44</td>
<td>1</td>
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<tr>
<td>Pre-evaluation</td>
<td>44</td>
<td>1</td>
<td>4</td>
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<tr>
<td>Evaluation</td>
<td>31</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lab testing (Phase I)</td>
<td>4</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Field studies (Phase I)</td>
<td>9</td>
<td></td>
<td>0</td>
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<tr>
<td>Field trials (Phase II)</td>
<td>15</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>103</td>
<td>245</td>
<td>4</td>
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</table>

### Health products in the pipeline

<table>
<thead>
<tr>
<th>Disease name</th>
<th>Product type</th>
<th>Product name</th>
<th>Phase of development</th>
</tr>
</thead>
<tbody>
<tr>
<td>African Trypanosomiasis</td>
<td>Diagnostics</td>
<td>HAT LAMP</td>
<td>Evaluation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HAT lateral flow (2nd gen.)</td>
<td>Evaluation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HAT Rapid Diagnostic Test</td>
<td>Evaluation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HAT/Malaria RDT</td>
<td>Evaluation</td>
</tr>
<tr>
<td>Medicines</td>
<td></td>
<td>Fexinidazole</td>
<td>Phase III</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fexinidazole (pediatric)</td>
<td>Phase III</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SCYX-7158 (AN5568)</td>
<td>Phase III</td>
</tr>
<tr>
<td>Antibiotic resistant bacteria</td>
<td>Medicines</td>
<td>Abacillin (Depio 1450)</td>
<td>Phase II</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aztreonam+Avibactam (A...)</td>
<td>Phase II</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Baxdela (delafloxacin)</td>
<td>Phase III</td>
</tr>
</tbody>
</table>
Clinical trials

Clinical trials from the WHO ICTRP data source

Can explored by:
- year,
- disease,
- phase of development,
- region or country

(data from 1999-2016)
Monitoring publications: exploring the data

- Users can select and deselect items to customize data output according to their interest.

- For instance, for dengue, users will see that there has been a steep increase in publications since 2000, with first authors centred in South America, Asia as well as the United Kingdom.
Upcoming:
Monitoring research grants: World RePORT

Exploring grants to low income countries

<table>
<thead>
<tr>
<th>WHO region</th>
<th>High income</th>
<th>Upper middle</th>
<th>Lower middle</th>
<th>Low income</th>
<th>Unknown</th>
<th>Grand Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>2085</td>
<td>1,978</td>
<td>1,290</td>
<td>962</td>
<td>5</td>
<td>74,426</td>
</tr>
<tr>
<td>Americas</td>
<td>61,164</td>
<td>5,831</td>
<td>31</td>
<td>24</td>
<td>5</td>
<td>63,830</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>8,124</td>
<td>94</td>
<td>37</td>
<td>17</td>
<td>5</td>
<td>8,510</td>
</tr>
<tr>
<td>Europe</td>
<td>2,085</td>
<td>1,978</td>
<td>1,290</td>
<td>962</td>
<td>5</td>
<td>74,426</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>602</td>
<td>515</td>
<td>31</td>
<td>24</td>
<td>5</td>
<td>74,426</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>80</td>
<td>80</td>
<td>27</td>
<td>26</td>
<td>5</td>
<td>74,426</td>
</tr>
</tbody>
</table>

Top recipient organizations

<table>
<thead>
<tr>
<th>Organization</th>
<th>Number of grants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Makerere University</td>
<td>101</td>
</tr>
<tr>
<td>MRC, Unit, The Gambia</td>
<td>56</td>
</tr>
<tr>
<td>MRC/LUVI Uganda Rese.</td>
<td>39</td>
</tr>
<tr>
<td>Muhimbili University</td>
<td>31</td>
</tr>
<tr>
<td>University of Malawi</td>
<td>27</td>
</tr>
</tbody>
</table>

© World Health Organization 2017 | Source: Global Observatory on Health R&D
(http://who.int/research-observatory/en/)
New Expert Committee on health R&D

- Requested by resolution WHA69.23 to advise the DG on new R&D priorities based on public health needs—within the same focus of diseases of the poor

- Closely linked to and draws from information and analysis provided by the R&D Observatory.

- Work ongoing to:
  - select and appoint experts (formal process)
  - produce comprehensive analyses of disease-specific R&D and
  - develop the methods for the priority setting process
Key messages

1. The R&D Observatory provides one comprehensive source of information and analyses on key health R&D activities
   – that is reviewed and quality assured by WHO

2. Priority setting for new R&D through the Expert Committee provides an independent, impartial and evidence-based approach to set global priorities based on public health needs

3. Added value of linking the two initiatives:
   – Common approach for priority setting across diseases
   – Coordination of efforts for priority setting across multiple initiatives
Acknowledging funding support

The Observatory gratefully acknowledges the financial support of (in alphabetical order since inception):

• European Commission
• Government of France
• Government of Germany
• Government of Switzerland
• Government of the United States of America

For more information: http://www.who.int/research-observatory/en/
Email: rd-observatory@who.int
An R&D Blueprint for action to prevent epidemics

TPPs & Data Sharing
Accelerating Research & Development Processes

A. Improving coordination & fostering an enabling environment

B. Accelerating R&D processes

C. Developing new norms & standards tailored to the epidemic context

R&D Roadmaps/TPPs
A generic methodology
Developing and implementing R&D Roadmaps for priority pathogens with epidemic potential

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

developed on the basis of

generic methodology

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

Cycle of review

→ Internal review – completed
→ Intermediate review – completed
→ External review – ongoing
→ Pilot testing for development of the following roadmaps (taskforce) – ongoing
  • Ebola/Marburg, Lassa and Nipah
  • CCHF
  • Pathogen X
## Development timeline for vaccine TPPs

<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>Circulation of draft TPP to Expert Working group for comments</th>
<th>Public consultation of draft TPPs</th>
<th>Final TPP published at WHO website</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monovalent Ebola – reactive and preventive use</td>
<td>✔</td>
<td>✔</td>
<td>2015</td>
</tr>
<tr>
<td>Multivalent filovirus vaccine TPP – preventive use</td>
<td>✔</td>
<td>✔</td>
<td>Nov 2016</td>
</tr>
<tr>
<td><strong>Revised</strong> Zika virus vaccine TPP (first version, published July 2016)</td>
<td>✔</td>
<td>✔</td>
<td>Feb 2017</td>
</tr>
<tr>
<td>MERS Co-V vaccine TPPs (3)</td>
<td>✔</td>
<td>✔</td>
<td>May 2017</td>
</tr>
<tr>
<td>Nipah Virus vaccine TPP</td>
<td>Q1</td>
<td>Q1</td>
<td>June 2017 (Finalization)</td>
</tr>
<tr>
<td>Lassa Fever virus vaccine TPP</td>
<td>Q1</td>
<td>Q2</td>
<td>June 2017 (Finalization)</td>
</tr>
</tbody>
</table>
MERS-CoV

• 3 vaccine strategies called for in roadmap - TPPs completed
  – Dromedary camel vaccine, human vaccine for preventive use, & human vaccine for reactive use

• A WHO-OIE-FAO global MERS-CoV technical meeting is planned for September 26-28, 2017 in Cairo, Egypt.

• Main objectives of the meeting:
  – new research and progress,
  – coordination between animal and public health sectors in outbreak preparedness and response,
  – surveillance and technical issues on disease control,
  – review recommendations based on latest scientific evidence
  – outline research priorities.
Lassa fever vaccine (Preventive Use)

Highest priority for development is for preventive use and TPP is focused on that scenario.

Some vaccine products may address both scenarios: preventive use, and outbreak control.

One possible strategy: vaccination where LF is hyper endemic and where clusters of cases are reported annually.

Indication: active immunization of persons considered potentially at risk based on risk factors to protect against Lassa fever
Status of vaccine research and development of vaccines for Nipah virus

Benjamin A. Satterfield, Brian E. Dawes, Gregg N. Milligan

Department of Microbiology and Immunology, University of Texas Medical Branch, Galveston, TX, United States
Department of Pediatrics, University of Texas Medical Branch, Galveston, TX, United States
WHO Collaborating Center, University of Texas Medical Branch, Galveston, TX, United States
# Development timeline for diagnostic TPPs

<table>
<thead>
<tr>
<th></th>
<th>Circulation of draft TPP to Expert Working group for comments</th>
<th>Public consultation of draft TPPs</th>
<th>Final TPP published at WHO website</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ebola virus</td>
<td></td>
<td></td>
<td>October 2014</td>
</tr>
<tr>
<td>Zika virus diagnostics(^2)</td>
<td>March 2016</td>
<td>22 March to 11 April 2016</td>
<td>April 2016</td>
</tr>
</tbody>
</table>

Planned for 2017: **Diagnostics Mapping**: MERS- CoV, CCHF, Lassa Fever and Nipah Virus
## Clinical trial registration/results policies: some highlights from Global perspective

<table>
<thead>
<tr>
<th>Year</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1986</td>
<td>First call for international registry (<a href="https://doi.org/10.1097/00000421-198612000-00033">Simes R J Clin Oncol 1986 4: 1529-1541</a>)</td>
</tr>
<tr>
<td>2000</td>
<td>ClinicalTrials.Gov launched</td>
</tr>
<tr>
<td>2005</td>
<td>WHA resolution on universal registration</td>
</tr>
<tr>
<td>2005</td>
<td>WHO International Clinical Trial Registry Platform (ICTRP) launched WHO minimum registration dataset agreed and endorsed by ICMJE – leads to massive increase in registration</td>
</tr>
<tr>
<td>2007</td>
<td>India and China registries join ICTRIP</td>
</tr>
<tr>
<td>2008</td>
<td>Updated Declaration of Helsinki mandated trial registration</td>
</tr>
<tr>
<td>2009</td>
<td>Pan African registry joins ICTRIP</td>
</tr>
<tr>
<td>2011</td>
<td>Brazilian registry joins ICTRIP</td>
</tr>
<tr>
<td>2013</td>
<td>Clear ethical requirement on results disclosure in Helsinki</td>
</tr>
<tr>
<td>2015</td>
<td>WHO launches position calling for public disclosure of results from all clinical trials – norm of 12 months from study completion date</td>
</tr>
</tbody>
</table>
Rationale for WHO 2015 position calling for prompt public disclosure of results from clinical trials

- 30-50% of all clinical trials remain unreported according to systematic reviews of over 100 studies on publication bias*
- Applies to large and small trials across all product classes examined
- Evidence that published literature overestimates efficacy and under-estimates harms (although bias can go in either direction for individual products)* & **
- Multiple concrete examples of harm related to non-disclosure of results and data, including deaths, billions of dollars of wasted research funding per year***, poorly allocated financing of available interventions, slower timelines for product development

- It is unethical to conduct human research without publication and dissemination of the results of that research.
  - Social and scientific benefits cannot accrue if the results are not made available.
  - Withholding results may subject future volunteers to unnecessary risk.

WHO position on registration and reporting

WHO ICTRP
Expanded from 20 to 24 data fields in May 2017

- Initial registration dataset
- Access to full protocol
- Summary results using registries
- Journal publication
- Access to full data set/clinical study report

WHO policy
Trial registry

ICTRP adding additional core data fields on ethics committee, completion date, trial protocol, results summaries, and a data sharing statement
18 May 2017: Joint statement on public disclosure of results from clinical trials

Develop and implement a policy within 12 months of signing with following elements:

• Prospective registration of all clinical trials including a monitoring component
• Specifying timeframe for results disclosure with monitoring
• Reporting of previous results to be included as “quality criterion” in assessment of new grants to PIs

**Signatories to Joint Statement**

Indian Council of Medical Research  
Inserm  
Norwegian Research Council  
UK DFID  
UK MRC  
Bill and Melinda Gates Foundation  
CEPI  

DNDi  
Institut Pasteur  
MMV  
MSF and its research arm Epicentre  
PATH  
Wellcome Trust
Editorials

The WHO joint statement from funders on trials transparency

_BMJ_ 2017; 357  doi: https://doi.org/10.1136/bmj.j2816

(Published 19 June 2017)

This new statement from non-industry funders is a model of best practice
<table>
<thead>
<tr>
<th></th>
<th>Low income</th>
<th>High income</th>
<th>Researchers</th>
<th>Funders</th>
<th>Manufacturers</th>
<th>Ethics/Regulatory</th>
<th>Medical Journals</th>
<th>Outbreak response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surveillance</td>
<td></td>
<td></td>
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<tr>
<td>Genetic sequence data</td>
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<td>Clinical trials</td>
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<td>Observation studies</td>
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<tr>
<td>Sample sharing/biobanking</td>
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</table>
Data Sharing: Next steps and priorities

• **Align funder policies & conditions**, including disclosure of clinical research results
• Develop & pilot mechanisms to **incentivize data sharing**
• Reach **consensus on definitions & models** of good practice around data-sharing in PHEs
• Develop **phased approaches to data sharing** during a PHE
Next steps and priorities

- Collaborating on a **code of conduct for rapid sharing of pathogen genome sequencing in outbreaks**
- Raising awareness of web portals that allow access to pre-publication information sharing (BioRxiv, F1000 research, others)
- Reaching out to organisations dedicated to sharing **results of pre-clinical trials**
- Follow up data sharing meeting planned for December 2017