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1. Introduction

The Intervention and Implementation Research (IIR) unit endeavours to cover a range of areas of research addressing some of the critical obstacles to achieving the Sustainable Development Goals (SDG) for health.

This report summarises the IIR workplan, achievements and future plans with respect to four main questions:

1. Which are the new tools that are critically needed to improve disease control and possible achieve elimination? This covers how to provide a directional perspective to new developments so that they generate the health solutions that disease-endemic countries need; and how TDR, through its convening power and its special positioning and close links with both research and disease control, help promote innovation to generate more adapted health solutions. These requirements have been exposed by the recent succession of outbreaks.

2. How can the current medicines be protected? Available effective interventions are few, and some diseases rely on a single drug for control, prevention and treatment. While drug resistance is inevitable, these precious drugs must be safeguarded to optimise their lifespan of effective use. Antimicrobial resistance is now a general concern worldwide, at all levels of country development. IIR’s current focus is on drugs used for mass drug administration, in particular for preventive chemotherapy for helminthiases, but the approach can be expanded to other diseases and drug classes.

3. How best can informed recommendations and policy decisions be made on the use of available health interventions? The evidence-base for a number of recommendations is weak due to a combination of insufficient research, insufficient standardisation of research methodologies and insufficient level of analysis of research results. Correcting these shortcomings is of paramount import, and is expected to translate into a more efficient use of resources and more informed directions for both research and disease control. TDR’s recognised convening power is applied to broker agreements across a range of stakeholders towards optimising the use of available data by sharing and analysing data.

4. How can effectively proven interventions be effectively deployed and adapted to achieve disease control and elimination objectives, while building sustainable in-country capacity and transfer empowerment to the concerned countries? A number of approaches are used, such as disease- and context-specific projects in support of defined programme objectives (e.g. the elimination of visceral leishmaniasis in the Indian subcontinent; sub-regional initiatives to achieve the objectives of the endTB strategy; outbreak preparedness for dengue and other arborviruses); and generally-applicable approaches to create in-country capacity for operational and implementation research.
2. Overall objectives and expected results

The workplan of the intervention and implementation research (IIR) unit covers the following four objectives:

1. Facilitate innovation
2. Sustain effectiveness of available interventions
3. Strengthen the evidence base for policy decisions
4. Optimize implementation of available interventions

Within these, there are ten expected results, some of which were modified in 2015 to increase emphasis on implementation/operational research projects, in coordination with the Scientific Working Group, as explained in the progress section.

3. Key research achievements

- **Data-sharing to optimise research investments and improve the evidence-base.** TB clinical trial data-sharing platform established, access will be granted from end of Q1 2016; initial database established for schistosomiasis and stakeholder consultations for data-sharing platform initiated. Activities conducted with partners and stakeholders. TDR role clearly defined as promoter, convener and facilitator in the initial phase, including strengthening endemic country capacities.

- **Support country elimination programmes.** Research in support of the attack phase of the visceral leishmaniasis (VL) elimination in the Indian Subcontinent (ISC) successfully completed in Nepal and Bangladesh; research to inform sustainable interventions for the consolidation and maintenance phase under way. All activities are conducted as a collaboration between country researchers and control programme managers and international collaborators.

- **Support country outbreak preparedness.** (i) Retrospective studies of alert signals for dengue outbreaks completed, which informed the prospective study that is now under way in 3 countries. (ii) Study design and approaches to generating evidence for infectious diseases with epidemic potential.

- **The Structured Operational/Implementation Research and Training Initiative (SORT IT).**
  - 4 standard 10-month SORT IT OR courses completed (48 participants); and two one-day courses on OR skills (173 participants).
  - SORT IT Phase 1 OR prioritization and capacity planning completed: national (8 countries: Colombia, Kenya, Liberia, Myanmar, Peru, Sierra Leone, Surinam and Ukraine) and sub-regional (Southern Africa).
  - SORT IT Phase 2 integrated OR and training courses completed: 2 sub-regional programmes (Central Asia and Latin America); started: national (4 countries: Kenya, Myanmar, Peru and Ukraine), sub-regional (Southern Africa). Completed the first formal training course on workshop facilitation skills for SORT IT Phase 2 facilitators.
  - SORT IT Phase 3 research dissemination: sub-regional programmes started (Central Asia and Latin America).
  - SORT IT Phase 4 issue briefs for policy (IBP): completed training of trainers workshop on evidence-informed policy-making. In partnership with WHO’s EVIPNet (the Evidence-Informed Policy Network), conducted an IBP Workshop for the Eastern Europe SORT IT Programme (8 participants completed a stakeholder mapping and created IBPs from their research papers).
  - The SORT IT partnership produced more than 70 manuscripts for submission to peer-reviewed journals in 2015.
4. Progress in 2015 and planned activities for 2016-17

The following ER table provides a quick overview of the structure as revised in 2014, and updates on meeting targets. (*) indicates changes made following the SWG recommendations. A narrative by objective is provided below.

### Expected results - Intervention and implementation research

<table>
<thead>
<tr>
<th>IIR Objective</th>
<th>Expected results by outcome</th>
<th>Indicators and targets</th>
</tr>
</thead>
</table>
| Objective 1: Facilitate Innovation | 1.1.5 Facilitate innovation to generate tools to achieve control programme objectives: i) awareness of specific gaps generated for funders, researchers and developers; ii) workable approaches (technologies, products, partnerships) identified and applied. | By 2015, at least two approaches identified.  
- On target: 1) data-sharing in emergencies; 2) data-sharing platforms for TB, schistosomiasis; 3) NTD website  
- Achieved: Moxidectin transferred to not-for-profit organization for registration |

| Objective 2: Sustain effectiveness of available interventions | 1.1.2 Integrated capacity building and research for ivermectin resistance surveillance: i) presence or absence of genetic correlates of suboptimal response of *O. volvulus* to ivermectin established; ii) tool for surveillance; iii) strategy approved, guidelines and training package for conduct of surveillance.  
1.1.3 Integrated capacity building and research for lab-to-field translation of putative resistance markers: i) capacities in DEC created (scientists trained, laboratories equipped); ii) putative resistance markers tested in the field  
1.1.4 Vulnerability to emerging drug resistance and its consequences for control programmes. Information on resistance of pathogens of tropical diseases to existing treatments and response options to inform control programme practice, research and funding decisions. | By 2014, proof-of-concept in the lab of genetic markers of putative ivermectin resistance.  
By 2015, tool for surveillance of resistance available.  
- Modified and merged with 1.1.4 (see below)*.  
- Delayed, due to timing of selection of new proposals to be funded.  
By 2015, at least two putative resistance markers tested in the field.  
- Not applicable anymore since cancelled in 2014* |

| Objective 3: Strengthen evidence base | 1.1.6 Knowledge to fill the gaps in control and elimination of tropical diseases: i) optimized, standardized methodologies to assess the effects of interventions; ii) databases from existing clinical trials generated and analysed to maximize the use of data and optimize the cost of clinical trials.  
1.1.7 Strengthen evidence-base for policy decision and programme implementation by maximising the utility of available data. Consolidated evidence platform necessary for WHO recommendations: evidence for policy recommendations including conclusions from efficacy and safety, as well as cost-effectiveness of interventions. | By 2015, at least two optimized, standardized methodologies generated; one database developed.  
- On target – merged with 1.1.7* |

By 2014, analysis of issues related to the availability, deployment and effectiveness of fluoroquinolones in tuberculosis delivered.  
- Modified and merged with 1.1.6* |
<table>
<thead>
<tr>
<th>IIR Objective</th>
<th>Expected results by outcome</th>
<th>Indicators and targets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective 3: Strengthen evidence base (cont.)</td>
<td>1.1.8 Safety data for policy decisions</td>
<td>By 2015, birth defect data related to drug exposure analysed, data presented to WHO treatment guidelines committees.</td>
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<td></td>
<td>Optimise the acquisition and analysis of new safety data for policy decision and programme implementation</td>
<td>• Delayed. Database finalized and ready for piloting but no data yet formally included. Sites expected to contribute new data in 2016 with first data analysis by end of 2016.</td>
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<td></td>
<td></td>
<td>By 2015, at least one project for monitoring safety established in countries</td>
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<td></td>
<td>• On target. Study on pharmacovigilance (PV) in seasonal malaria chemoprevention completed, study on PV in mass drug administration in preparation.</td>
</tr>
<tr>
<td>Objective 4: Optimize implementation</td>
<td>1.1.1 Support adequate country response to epidemic challenges: evidence-based guidance for dengue outbreak detection and response.</td>
<td>By 2016, field trials to test novel tools completed.</td>
</tr>
<tr>
<td></td>
<td>1.2.1 Intervention and implementation research to inform policies for the elimination of visceral leishmaniasis. Evidence generated to inform policies for the elimination of visceral leishmaniasis in the Indian subcontinent: i) cost-effectiveness of camp approach under programmatic conditions; ii) vector control and improved monitoring and evaluation toolkit; iii) methods to identify VL cases adapted to low-endemic areas; iv) cost and feasibility of using liposomal amphotericin B at peripheral health service level</td>
<td>• On target. Retrospective study completed, prospective study under way.</td>
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<tr>
<td></td>
<td>1.2.2 Community-based scheduled screening and treatment of malaria in pregnancy for improved maternal and infant health (COSMIC).</td>
<td>By 2016, studies in Bangladesh, India and Nepal on case detection and case management completed</td>
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<td></td>
<td></td>
<td>• Delayed but under way. Expected completion of studies and data analysis: Q4 2016.</td>
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<td>• Output iv and proposed linked activities cancelled.</td>
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<td></td>
<td>1.2.3 Improved management of childhood febrile illnesses. Evidence on improved management of childhood febrile illnesses: i) number of severe patients who respond immediately and can be adequately managed without referral, ii) evidence on when not to treat with an antibiotic, iii) evidence on reliability of RDT use in severe disease, iv) evidence for strengthening compliance with referral advice</td>
<td>By 2015, methods developed to inform stakeholders and secure commitment to facilitate policy and practice changes</td>
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<td></td>
<td></td>
<td>• No-cost extension requested by consortium, potential delay to Q2 2017</td>
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<tr>
<td></td>
<td>1.2.4 Structured Operational/Implementation Research and Training Initiative (SORT IT). Outcome-oriented, policy-relevant, integrated operational/implementation research and training that is embedded within the public health programmes of low- and middle-income countries designed and delivered for tuberculosis and other diseases.</td>
<td>By 2015, measurements on sensitivity, specificity of RDTs/microscopy for severe disease, and changes in RDT outcomes for patients evolving to severe malaria generated.</td>
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<tr>
<td></td>
<td></td>
<td>• Indicator modified to reflect focus on febrile illnesses in young infants and evidence for antibiotic treatment: By 2017, evidence for antibiotics management. On target.</td>
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<tr>
<td></td>
<td></td>
<td>• Cancelled: Output i, ii and iv were dropped to free resources for output iii (febrile illnesses in young infants per ad hoc Scientific Advisory Group (SAG) recommendation in February 2014).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>By 2015, at least 20 integrated operational/implementation research projects in countries.</td>
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<td>• On track.</td>
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<td></td>
<td></td>
<td>• Over 140 operational research projects completed in all 5 regions (over 50 countries). Over 100 OR projects started in 2015 in over 25 countries (all 5 regions).</td>
</tr>
</tbody>
</table>
## 5. Updated 2016-17 workplan

<table>
<thead>
<tr>
<th>ER</th>
<th>2014-15</th>
<th>2016-17</th>
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</thead>
<tbody>
<tr>
<td><strong>Facilitate innovation</strong></td>
<td></td>
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<tr>
<td>1.1.5</td>
<td>Facilitate innovation to generate tools to achieve control programme objectives</td>
<td>Facilitate innovation to generate tools to achieve control programme objectives</td>
</tr>
<tr>
<td><strong>Sustain intervention effectiveness</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1.4</td>
<td>Vulnerability of preventive chemotherapy programmes for helminths to emergence of resistance</td>
<td>Strategies for surveillance/early detection of malaria drug resistance in seasonal malaria chemoprevention areas</td>
</tr>
<tr>
<td>1.1.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Strengthen evidence base for WHO recommendations and country policies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1.7</td>
<td>Strengthen evidence-base for policy decision and programme implementation by maximizing utility of available data</td>
<td>Maximize the utility of available data for policy decisions and programme implementation</td>
</tr>
<tr>
<td>1.1.8</td>
<td>Safety data for policy decision</td>
<td>Optimize acquisition and analysis of new safety data for policy decisions and programme implementation</td>
</tr>
<tr>
<td><strong>Optimize implementation of available interventions and strategies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.2.4</td>
<td>Structured Operational Research and Training Initiative (SORT IT)</td>
<td>Structured Operational Research and Training Initiative (SORT IT)</td>
</tr>
<tr>
<td>1.2.2</td>
<td>Strategies to accelerate research-policy transition (COSMIC)</td>
<td>Strategies to accelerate research-policy transition (COSMIC)</td>
</tr>
<tr>
<td>1.1.1</td>
<td>Support adequate country response to epidemic challenges: evidence-base guidance for dengue outbreak detection and response</td>
<td>Research in support of control programmes: Arboviruses outbreak response</td>
</tr>
<tr>
<td>1.2.3</td>
<td>Improved management of febrile illnesses</td>
<td>Research in support of control programmes: Improved management of febrile illnesses</td>
</tr>
<tr>
<td>1.2.6</td>
<td></td>
<td>Research in support of control programmes: TB control in line with Global TB control strategy</td>
</tr>
<tr>
<td>1.2.1</td>
<td>Research in support of elimination programmes VL elimination in the Indian sub-continent</td>
<td>Research in support of elimination programmes VL elimination in the Indian sub-continent</td>
</tr>
<tr>
<td>1.2.7</td>
<td>if 55 M (Research in support of elimination programmes: onchocerciasis elimination)</td>
<td></td>
</tr>
<tr>
<td>1.2.5</td>
<td>if 55 M (Translating new and traditional knowledge into healthy environmentally sustainable housing)</td>
<td></td>
</tr>
</tbody>
</table>
### 6. Status of activities: 2016-17 workplan vs. 2014-15

<table>
<thead>
<tr>
<th>FACILITATE INNOVATION</th>
<th>COMPLETED</th>
<th>CONTINUING</th>
<th>EVOLVING</th>
<th>NEW</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Facilitate R&amp;D and innovative R&amp;D approaches</strong></td>
<td>Moxidectin transfer for registration</td>
<td>Assist organizations involved in R&amp;D</td>
<td>Assist international response to epidemic diseases (WHO R&amp;D Blueprint; global health security)</td>
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<tr>
<td><strong>SUSTAINED INTERVENTION EFFECTIVENESS</strong></td>
<td>Vulnerability of NTD preventive chemotherapy programmes to emergence of resistance</td>
<td>Genetic markers of response of O. volvulus to ivermectin</td>
<td>Seasonal malaria chemoprevention</td>
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<tr>
<td>Strategies for surveillance/early detection of drug resistance in mass drug administration</td>
<td>Variability of response to drugs before/early during MDA</td>
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<tr>
<td><strong>STRENGTHEN THE EVIDENCE-BASE FOR WHO RECOMMENDATIONS</strong></td>
<td>Maximise utility of available data:</td>
<td>Cutaneous leishmaniasis trial standardisation</td>
<td>Data-sharing platforms: TB clinical trials; schistosomiasis research &amp; control programme data; cutaneous leishmaniasis trials; SORT IT networks</td>
<td></td>
</tr>
<tr>
<td>Optimize acquisition and analysis of new safety data for policy decisions and programme implementation:</td>
<td>Pilot pregnancy registry</td>
<td>Capacity building for safety monitoring (with WHO/EMP technical support)</td>
<td>Innovative approaches for safety monitoring: low-dose primaquine for malaria elimination (only if US$ 55M budget)</td>
<td></td>
</tr>
<tr>
<td><strong>OPTIMIZE IMPLEMENTATION OF AVAILABLE INTERVENTIONS AND STRATEGIES</strong></td>
<td>Capacity building for implementation research: SORT IT</td>
<td>Work closely with ministries of health, external (CDC, EIPNet, MSF, Union and academic institutes) and WHO partners (GTB, GMP, WHO Regional Offices)</td>
<td></td>
<td>Franchising out SORT IT</td>
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<td></td>
<td></td>
<td>Accent on research prioritization and getting evidence into policy/practice cover TB, malaria, NTDs - Drive SORT IT to national level activities led by Ministries of Health and national partners</td>
<td>Leadership development – SORT IT Fellows</td>
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<tr>
<td></td>
<td></td>
<td>Introduction more complex research into programmes, align SORT IT within One-TDR approach</td>
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<tr>
<td>Research in support of disease control</td>
<td>COMPLETED</td>
<td>CONTINUING</td>
<td>EVOLVING</td>
<td>NEW</td>
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<tr>
<td>* Assist TB national programmes in achieving GTB end-TB strategy (in collaboration with WHO/GTB, WHO/IST): IR and intensified case-finding by West African national TB programmes</td>
<td>* Arboviruses outbreak detection and response by control programmes</td>
<td>* SORT IT Programmes covering control of malaria, tuberculosis, NTDs and other diseases of public health importance in countries and sub-regions of Europe, Africa, Asia and the Americas</td>
<td>* Translating new and traditional knowledge into healthy environmentally sustainable housing (only if US$ 55M budget and designated funds)</td>
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<table>
<thead>
<tr>
<th>Research in support of disease elimination</th>
<th>COMPLETED</th>
<th>CONTINUING</th>
<th>EVOLVING</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Visceral leishmaniasis elimination in the Indian subcontinent – support national control and research in the attack phase</td>
<td>* Feasibility of vector control to accelerate lymphatic filariasis (LF) elimination (funded via SDF)</td>
<td>* Visceral leishmaniasis elimination in the Indian subcontinent: support national control and research in the consolidation &amp; maintenance phases</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Support transfer of research results to policy</th>
<th>COMPLETED</th>
<th>CONTINUING</th>
<th>EVOLVING</th>
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<tbody>
<tr>
<td>* Community-based scheduled screening and treatment of malaria in pregnancy for improved maternal and infant health (COSMIC)</td>
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| | | | |
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## 7. Disease spectrum covered by IIR activities

<table>
<thead>
<tr>
<th>FACILITATE INNOVATION</th>
<th>Malaria</th>
<th>Schistosomiasis and STHs</th>
<th>Onchocerciasis &amp; lymphatic filariasis</th>
<th>Leishmaniasis (visceral &amp; cutaneous)</th>
<th>Dengue</th>
<th>Emerging epidemics</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tuberculosis</td>
<td></td>
<td>* Moxidectin transfer and preparation for implementation studies</td>
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<tr>
<td>SUSTAINED INTERVENTION EFFECTIVENESS</td>
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<td></td>
<td>* Variability of response before/early during MDA</td>
<td>* Genetic markers of response of O. volvulus to ivermectin</td>
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<td></td>
<td></td>
<td>* Variability of response to drugs before/early during MDA</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>* Models of transmission of parasites with low susceptibility/resistance to drugs</td>
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<tr>
<td>STRENGTHEN THE EVIDENCE-BASE FOR WHO RECOMMENDATIONS</td>
<td>* Central database for safety data from active drug safety monitoring of MDR-TB drugs</td>
<td>* Standardise treatment outcome measures</td>
<td>* Standardise treatment outcome measures</td>
<td>* Cutaneous Leishmaniasis trial standardisation</td>
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</table>
### OPTIMIZE IMPLEMENTATION OF AVAILABLE INTERVENTIONS AND STRATEGIES

<table>
<thead>
<tr>
<th>Tuberculosis</th>
<th>Malaria</th>
<th>Schistosomiasis and STHs</th>
<th>Onchocerciasis &amp; lymphatic filariasis</th>
<th>Leishmaniasis (visceral &amp; cutaneous)</th>
<th>Dengue</th>
<th>Emerging epidemics</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase TB detection: TB, HIV and diabetes national programmes</td>
<td>Central registry for epidemiological surveillance of drug safety in pregnancy (with HIV)</td>
<td>SORT IT Programme for malaria elimination in Southern Africa</td>
<td>COSMIC, methods developed to inform stakeholders and secure commitment to facilitate policy and practice changes.</td>
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<tr>
<td>MDR-TB: SORT IT; support Practecal trial</td>
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- Dengue}

- Visceral leishmaniasis elimination in the Indian subcontinent
Objective 1: Facilitate innovation

The dearth of products currently available to diagnose, treat and prevent neglected tropical diseases (NTDs) and infectious diseases of poverty at large is fundamentally due to a lack of innovative products and approaches to develop, test and deploy them efficiently. While TDR has moved away from direct involvement and sponsoring of research and development projects, it is using its convening power, expertise and connections with both researchers and control programmes to help identify and test innovation.

EXPECTED RESULT 1.1.5: FACILITATE INNOVATION TO GENERATE TOOLS TO ACHIEVE CONTROL PROGRAMME OBJECTIVES

There are five expected results, one of which is new and was added in response to the Ebola outbreak.

1. Promote and facilitate open-source, open-access approaches

Context and rationale: Reasons why IIR is actively involved in this area:

- Responding to researchers’ and countries’ requests: TDR reputation as trusted broker and convener.
- Responding to policy-makers’ needs to strengthen the evidence-base to inform recommendations/guidelines (see 1.1.7) and the design of future trials. This provides advantages of individual participant-level data over aggregated-data meta-analysis for evidence generation.
- Responding to and supporting WHO policies and research funders’ and publishers’ requirements that researchers align on data-sharing obligations.

Progress in 2015

Significant progress has been made with data-sharing initiatives. All objectives have been attained, and further expanded (see also 1.1.7).

Activities conducted in 2015 in support of data-sharing and open-source initiatives.

- TB and schistosomiasis data-sharing stakeholders meetings (http://www.who.int/tdr/news/2015/report-schisto-meeting-3-4Sept2015.pdf?ua=1; see also 1.1.7) in close collaboration with WHO/Global TB and WHO/NTD, respectively
- NTD website for sharing research tools active (see https://globalntdresearch.tghn.org/)
- SORT IT open access. All publications from SORT IT programmes now published in open access peer-reviewed journals. Where possible the products of a SORT IT Programme are published in a special supplement of a journal with papers published in the most appropriate languages. A supplement from the Eastern Europe SORT IT Programme was published in English and Russia in Public Health
Action. The papers from the Central Asia SORT IT Programme is currently in press in a Russian/English supplement of Public Health Panorama – the journal of the WHO Regional Office for Europe. An English/Spanish supplement of the Pan-American Health Journal featuring the products of the Latin American and Caribbean SORT IT Programme is currently in press.

Remaining challenges:

- Better understanding of elements that impede or inhibit data-sharing and identify solutions. Engage in dialogues with stakeholders.
- Enhance researcher’s confidence by offering ‘trustworthy’ environments.
- TDR to help design approaches, set up processes and identify sustainable solutions, and provide concrete examples of tangible solutions. After the initial phases, TDR cannot support initiatives in the long-term. Path-finding TDR’s way-in and way-out.

Plans for 2016

- Advocate on a bigger scale, help create an enabling environment that could be more widely applied by others.
- Activate access to the tuberculosis trial platform; advance schistosomiasis/soil-transmitted helminths (STH) data-sharing initiatives; further explore cutaneous leishmaniasis (CL) data-sharing options (see 1.1.7).
- Continue support data-sharing initiatives in public health emergencies/outbreaks.
- Publish and share TDR experience in data sharing.
- Training course in data sharing and analysis developed (joint IIR/RCS activity) in collaboration with GTB, WHO EURO and Liverpool School of Tropical Medicine. To be piloted in February 2016 in Turkey (for Eastern Europe and Central Asia SORT IT network). Discussions are under way with WHO/GTB as to how to include this SORT IT Network in safety monitoring of new TB drugs in 2016.
- TDR will continue to support the Eastern Europe and Central Asia SORT IT Network in its data-sharing ambitions following training in February 2016. TDR will also support two other regional SORT IT networks to develop data-sharing capacity in 2016: the Latin American and Caribbean Network and the Southern Africa Network. The training course piloted in February 2016 will be rolled out (with any required modifications) to these two additional networks.

2. Generate optimised methodologies to assess the effects of interventions for NTDs

Context and rationale: Reasons why IIR is actively involved in this area:

- Responding to the need for innovation in methodological approaches for poverty-related infectious diseases. Research methodologies are often ill-adapted to generate reliable evidence and not standardised enough.
- TDR reputation and convening power.

Progress in 2015

Cutaneous leishmaniasis (CL)

Activities in collaboration with Drugs for Neglected Diseases initiative (DNDi) and with the involvement of WHO/NTD:
• Call for expression of interest in defining core entry criteria and core outcome measures for CL to engage the CL research and health care provider community through a collaborative effort into: an online discussion process using Delphi methodology, combined with patient interviews: 8 investigators selected funded and trained in qualitative research.

• Dissemination of CL trial guidance document published in 2013 in Latin America through the researchers network RedLeish with DNDi.

Remaining challenges:

• Challenges inherent in pioneering a new approach, especially in patient’s involvement. CL is used as a test-case to generate evidence of models that can be more widely applied to other cases by other researchers.

Plans for 2016

• Complete the Delphi survey.

• Patient’s interviews: additional training on analysing qualitative data; analyse data and communicate results.

• Update CL trial methodology guidance document as needed.

• Disseminate CL trial guidance document and train researchers studying Old-world CL (OWCL) at a workshop at the TDR-supported Institut Pasteur Tunis Regional Training Centre.

3. Facilitate the development & registration of key products for public-health needs

Context and rationale: While TDR is no longer directly involved with product R&D, IIR continues to foster innovation and provide directionality and support to R&D of products to address priority public health needs.

Progress in 2015

In 2015, IIR conducted activities that respond to specific needs expressed by the relevant WHO departments: facilitate paediatric praziquantel as a treatment against schistosomiasis for young children, test new interventions for Ebola, and inform diagnostics R&D for taeniasis/cysticercosis and dengue. In addition, the transfer of moxidectin for onchocerciasis was successfully completed and leveraged external significant funds for its registration.

Onchocerciasis control and elimination: Transitioning of moxidectin from development by TDR to registration and implementation research by a not-for-profit organization.

• Transitioning completed. TDR led and managed the clinical development of moxidectin for onchocerciasis control and elimination initially in collaboration with a pharmaceutical company which later withdrew from the collaboration. In 2015 TDR successfully completed the transitioning of the project to the Australian not-for-profit organization Medicine Development for Global Health (MDGH). This allowed MDGH to raise US$ 10 million for the work required to ‘translate’ the TDR investment into moxidectin into registration, the prerequisite for moxidectin becoming available to countries.
• Dissemination of the results of moxidectin studies: (i) modelling of the Phase 2 study data to determine the potential impact of moxidectin on onchocerciasis elimination published\(^1\). It shows that: (1) annual moxidectin mass drug administration could accelerate progress towards elimination of onchocerciasis to a degree similar to that of biannual ivermectin but with significantly lower personnel requirements and cost to countries (provided moxidectin is donated); (2) moxidectin will provide particular advantages in areas with highly seasonal transmission. (ii) Phase 3 trial results publication delayed as MDGH are finalising regulatory report.

Remaining challenges: (i) Dissemination of moxidectin Phase 3 trial results; (ii) Assess issues and effects of deploying moxidectin through preventive chemotherapy at disease control programme level – how to design and conduct implementation research to answer these questions.

Schistosomiasis: Technical advice for the development of a paediatric formulation of praziquantel. WHO has identified preschool-aged children as a target group for schistosomiasis control, but the current praziquantel formulation is not adapted to small children. IIR and WHO/NTD continue to interact with the Pediatric Praziquantel Consortium on the development of paediatric praziquantel for schistosomiasis (for the time being still in parallel racemate and enantiomerically pure L-praziquantel). IIR is leading meta-analyses (unpublished; paper planned for 2016) to inform decisions, in particular vis-à-vis praziquantel optimal dosage in preschool-aged children (contribution to the “Informal consultation on treatment of Schistosomiasis in preschool-age children and pediatric Praziquantel formulations” WHO/HQ/Geneva, 29-30 September 2015).

Remaining challenges: Meaningful information for policy decisions requires gathering individual patient-level data (see 1.1.7)

Ebola Virus Disease. TDR was asked to: (i) support WHO/HIS by training on study procedures and Good Clinical Practices of Guinean staff involved in the vaccine trial sponsored by WHO - training of 170 study staff delivered by IIR in April 2015; and (ii) support the Secretariat of the WHO Ethics Review Committee in training members of the Ethics Committees in Liberia, Sierra Leone and Guinea.

Remaining challenges: Activity completed.

Facilitation of the development of and implementation research for diagnostic tools for prevention, control and elimination of NTDs. This activity was added in 2015 to facilitate the design, development and implementation research of adapted diagnostics in support of disease control and elimination.

• Taeniasis/cysticercosis
  o Context: Since the 2014 WHO informal consultation on taeniasis/cysticercosis, some countries have started to implement control programmes but need easy-to-use and inexpensive laboratory diagnostics to establish a baseline in order to measure the impact of interventions and to carry out regular surveillance. Currently there is no ideal diagnostic toolbox for use in low-resource settings that suit available resources and infrastructure, and that could form part of pilot interventions.
  o IIR activities: A consultation was organized in December 2015 jointly with WHO/NTD, gathering key countries implementing pilot control programmes and diagnostics researchers. The aim was to find a pathway to respond to the needs of countries with regard to advancing diagnostics.

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\(^1\) Turner HC, Walker M, Attah SK, Opoku NO, Awadzi K, Kuesel AC et al.: The potential impact of moxidectin on onchocerciasis elimination in Africa: an economic evaluation based on the Phase II clinical trial data. *Parasit Vectors* 2015, 8: 167
- Remaining challenges: Identifying how to use these results to leverage investments in adapted dengue diagnostics by developers and funding agencies.

- Dengue
  
  - Context: Current testing methods currently used to detect dengue virus (DENV) have limitations in terms of performance and usability. In order to assess the current state of DENV diagnostics and to develop a roadmap for the way forward to effective diagnostics for DENV for clinical management, surveillance and research, it is necessary to understand the current diagnostics landscape in terms of existing technologies as well as the test/technologies in the pipeline (including biotech concepts in the initial phase and/or at the stage of proof-of-concept). This would allow us to: (i) determine gaps in the current diagnostic landscape; (ii) map promising technologies; (iii) develop Target Product Profiles (TPPs) for the ideal diagnostics to detect DENV; and (iv) define key partners, particularly private sector partners, with whom to work in the development of new assays.

  - IIR activities: A landscape analysis of diagnostic technologies to detect dengue virus (DENV) to map and systematize the diagnostic tests and technologies to detect DENV that are currently available or in the pipeline. This will serve as the basis for developing a roadmap for the development of “ideal” diagnostic assays for dengue detection. This ultimately will lead to the definition of the Target Product Profiles for DENV diagnostics for clinical management, surveillance and research.

  - Remaining challenges: How to use these results to leverage investments in adapted dengue diagnostics by developers and funding agencies.

- Onchocerciasis
  
  - Context: Onchocerciasis endemic countries are now targeting not only control of onchocerciasis as a public health problem (i.e. elimination of morbidity), but also elimination of transmission where feasible. Areas with long-term ivermectin treatment with satisfactory geographic and treatment coverage require surveys for the prevalence of patent infection to assess their progress towards elimination. In addition, the prevalence of patent infection in hypo-endemic areas needs to be determined, because low-prevalence areas are currently not included in control activities. The DEC diagnostic skin patch was adopted by the Onchocerciasis Control Programme in West Africa (OCP) for surveillance purposes. The OCP utilized a patch prepared ad hoc as a suspension of diethylcarbamazine in Nivea cream. At the request of TDR, a company (Lohmann Therapie Systeme, Germany) specializing in transdermal delivery of drugs developed a new patch2 for this purpose.

  - IIR activities: To prepare for implementation research studies, IIR provided technical input for a training video on the application of the patch and provided funds for a batch to be used in upcoming implementation research studies (funded by TDR and others).

  - Remaining challenges: Determine how best to deploy the DEC patch within strategies for measuring progress towards elimination of onchocerciasis, including how to design and conduct implementation research to answer these questions.

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Plans in 2016

- **Onchocerciasis control and elimination**: (i) IIR to publish and disseminate moxidecitin phase 3 trial results; (ii) all moxidecitin and DEC patch-related activities will be technical advice to sponsors and investigators in support of implementation research for alternative treatment strategies that accelerate progress towards elimination of onchocerciasis. This maximizes the probability that TDR and control programme investments into both products will result in implementation of improved tools for onchocerciasis control and elimination.

- **Praziquantel for preschool-aged children**: Continue to provide evidence to inform adequate dosing of praziquantel in younger children (see 1.1.7).

- **Diagnostics**: Complete the review of published and unpublished (grey) literature and the report results for dengue. Develop a broader agenda for the role of diagnostics in achieving control and elimination objectives.

4. **Response to Control Programme requests for TDR input**

**Context and rationale**: TDR should be able to respond to specific control programme needs.

**Progress in 2015**

- **Onchocerciasis**
  - **Context**: Onchocerciasis endemic countries are now targeting not only control of onchocerciasis (i.e. elimination of morbidity), but also elimination of transmission where feasible.
  - **IIR activities**: At the request of the African Programme for Onchocerciasis Control (APOC), IIR contributed to the development of ‘alternative treatment strategies’ for onchocerciasis endemic areas where annual community-directed treatment with ivermectin (CDTI) is not possible (e.g. onchocerciasis hypoendemic areas with high prevalence of Loa loa infection). This supports further progress towards the goal of onchocerciasis elimination by 2025.
  - **Remaining needs/challenges**: Dissemination of results.

**Plans for 2016**

Dissemination/publication of results; no follow-up activities except in the case of WHO or programmes’ ad-hoc requests for TDR input.

5. **Technical support for Ebola and other epidemic diseases**

**Context and rationale**: Health emergencies pose challenges that must be acted upon quickly, and TDR should be able to mount a rapid response to specific control programme needs. However, some of the difficulties faced are avoidable if adequate research is conducted and sufficient in-country capacity is built in the inter-epidemic periods. In 2014-15 the world faced the worst Ebola epidemic ever. TDR was called upon to contribute and IIR responded through contributions to trial methodologies and post-EVD support in countries (See SORT IT). Based on the lessons learnt IIR is building a longer-term approach to support low and middle-income country capacity for research in epidemics.
Progress in 2015

Continuing contributions (mostly in collaboration with the University of Oxford) to:

- the development of a platform for testing Ebola virus disease (EVD) treatments in West Africa led by the University of Oxford. This included clinical trials of putative treatments: two drugs were tested: brincidofovir in Liberia (study terminated due to lack of cases and manufacturer withdrawal); TKM-Ebola in Sierra Leone (study reached the futility endpoint) – both submitted for publication, primary data sharing under way.


- supporting the development of a research framework for infectious diseases with epidemic potential, including support to WHO-led steering committees (Scientific and Technical Advisory Committee on Emergency Ebola Interventions STAC EE) and other meetings, including research (WHO Ebola R&D Summit, Geneva 11-12 May 2015) data-sharing (WHO, Geneva 1-2 September 2015) and ethics (Global Forum on Bioethics in Research Meeting (GFBR), Anncy 3-4 November 2015; and 28-29 October 2015, New York Academy of Sciences).

- the development of the WHO Blueprint for R&D preparedness and rapid research response (led by WHO/HIS) – building an R&D line of defence for global health threats (in conjunction with TDR’s research capacity strengthening and knowledge management unit (RCS/KM).

- raising the profile of research on infectious diseases with epidemic potential in the global agenda.

- TDR contributed to the first description of post-EVD conditions in survivors in the West African EVD epidemic. A description of the common conditions affecting EVD survivors in Kenema District, Sierra Leone, was described on the WHO website as soon as results were available. They were formally published in 2015.

- TDR, in collaboration with the Ministries of Health, WHO Country Offices, the International Union Against Tuberculosis and with financial support from DFID, has led the development of SORT IT Programmes in Sierra Leone and Liberia. These programmes are designed to support the national post-Ebola recovery plans for health systems in each country. The focus is on assessing the current state of the major public health and disease control services, including tuberculosis, malaria, HIV, EVD survivors, outbreak surveillance and control, maternal and child health services (including immunization). SORT IT Phase 1 (research prioritization and selection of trainees) has already been completed in each country, Phase 2 (integrated operational research and training) began in January 2016. A similar TDR-funded SORT IT Phase 2 in Guinea has been postponed to allow urgent vaccination campaigns for measles and polio to be completed, Phase 1 in Guinea has been completed and Phase 2 began in Guinea in late February 2016.

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**Remaining challenges:** More epidemic challenges are ahead with the MERS-CoV and Zika outbreaks and the long-lasting impacts from the Ebola epidemic. The WHO R&D Blueprint is under construction; global health security is a major priority and TDR has a role to play, but an adequate response will require sufficient human and financial resources. Furthermore, as explained above, TDR is not an emergency-response organisation, and works through building sustainable capacity for response. For this reason, for instance, the Zika response is integrated in a broader Arboviruses response which builds upon years of experience and work with countries on dengue by IIR and VES (see 1.1.1 below):

**Plans for 2016**

Continue contribution to the WHO R&D Blueprint with WHO/HIS, in particular: develop a toolkit to support investigators to conduct clinical research during outbreaks of infectious diseases, with a focus on providing tools that have utility for users with limited clinical research experience in low- and middle-income countries.

**Objective 2: Sustain effectiveness of available interventions**

**EXPECTED RESULT 1.1.4 VULNERABILITY TO EMERGING DRUG RESISTANCE AND ITS CONSEQUENCES FOR CONTROL PROGRAMMES (MERGED WITH 1.1.2 INTEGRATED CAPACITY BUILDING AND RESEARCH FOR IVERMECTIN RESISTANCE SURVEILLANCE).**

**Context and rationale:** The initial focus of this area is onchocerciasis with a view toward building the basis for further work in other helminthic diseases. In 2015 IIR also added work on malaria, to complement work being done on the safety of drugs deployed under Seasonal Malaria Chemoprevention (SMC, see 1.1.8). TDR initiated this research because understanding the vulnerability of mass drug administration (MDA)-based programmes to drug resistance is critical for developing appropriate strategies to safeguard achievements and continue progress towards control and elimination goals, and because this area of work is not being funded by others.

**Progress in 2015**

**Helminths.** Building on the work funded in past biennia, a multi-pronged synergistic approach has been put in place. The focus is now on *O. volvulus*, with extension to other helminthic diseases planned and initiated.

- **Quantification of the inter-subject variability of helminths’ response to the drugs used to control them before long term exposure to these drugs.**
  
  o **Context and rationale:** The efficacy data in the ivermectin arm of the Phase 3 study of moxidectin for treatment of onchocerciasis suggested that characterization of response to ivermectin via summary statistics is not a suitable basis for assessing emergence of parasite strains with low susceptibility to the drugs used in their preventive chemotherapy.
  
  o **IIR activities:** Research to quantitate the inter-subject variability of the response of helminths (schistosomiasis, lymphatic filariasis, STH and onchocerciasis) to the drugs used to control them before and early in MDA.
  
  o **Remaining challenges:** These will be determined based on the results in 2016-17 biennium.
• Development of parasite transmission models that can model the spread of parasites with low drug susceptibility within and between parasite and human populations.
  
o  **Context and rationale:** The extent to which parasite strains with low drug susceptibility jeopardize control/elimination programme objectives depends on the probability that they become more frequent and widespread. Models are needed which can estimate their transmission and the effect on intervention effectiveness, including alternative treatment strategies.
  
o  **IIR activities:**
  
  ▪ Two modelling groups with complementary expertise (*O. volvulus* transmission, population genetics, transmission of other infectious diseases) are collaborating on developing suitable models.
  
  ▪ A literature review was completed of the determinants of *O. volvulus* and *W. bancrofti* transmission and response to the preventive chemotherapy drugs, which is providing data for model development.
  
o  **Remaining challenges:** These will be determined based on results in 2016-17 biennium.

• Genetic markers of *O. volvulus* response to ivermectin.
  
o  **Context and rationale:** This research was initiated previously in response to 'suboptimal responses' of *O. volvulus* to ivermectin potentially indicating emerging resistance. The objective is to assess whether 'suboptimal response' is a heritable trait and if yes, to identify genetic markers to monitor the prevalence of 'suboptimal responders'.
  
o  **IIR activities:**
  
  The research now focuses on the validation of potential genetic markers identified previously, which requires collection of new parasite samples. The protocol received ethical approval in 2015.
  
o  **Remaining challenges:** (i) These will be determined based on results in 2016-2017 biennium; (ii) expansion to other helminthic diseases.

• Genetic markers of *O. volvulus* transmission zones.
  
o  **Context and rationale:** Onchocerciasis is now targeted not only for control as a public health problem, but also elimination of transmission. The decision to stop ivermectin distribution in one area can only be made when it is certain that it does not belong to the same 'transmission zone' as neighbouring areas where infection prevalence is still too high to stop ivermectin distribution. Current methods to determine transmission zones are based on vector species and cytogenetics which require a central laboratory. Genetic markers could provide a simpler, potentially field usable, tool.
  
o  **IIR activities:**
  
  ▪ Building on the results of the research for genetic markers of *O. volvulus* response to ivermectin, research for parasite genetic markers of transmission zones was initiated.
  
  ▪ Research on the feasibility of using the methodology developed for identification of genetic markers for vector species and lymphatic filariasis (LF) was initiated.
  
o  **Remaining challenges:** These will be determined based on results in the 2016-2017 biennium.
• **Synergistic activities funded through the Director's Strategic Development Fund (SDF)**

  o **Research capacity strengthening for modelling in the laboratories funded by TDR within the expected result 1.1.4: Vulnerability to emerging drug resistance and its consequences for control programmes**
    
    ▪ **Context and rationale:** Modelling is becoming more and more important and capacity in developing countries is limited.
    
    ▪ **Initiated in collaboration with research capacity strengthening (RCS) unit:** A new type of fellowship was piloted: Two junior researchers (one from the laboratory at Noguchi collaborating in the projects 'Genetic markers of *O. volvulus* response to ivermectin, Genetic makers of *O. volvulus* transmission zones', another from Tanzania) are spending one year in the two laboratories funded for the 'Development of parasite transmission models able to model the spread of parasites with low drug susceptibility within and between parasite and human populations'. Implementation of this fellowship is managed by the RCS unit.
    
    ▪ **Remaining challenges:** Review feedback with RCS from fellows and hosting institutions after the fellowship conclusion in 2016 and develop a recommendation on whether such fellowships should be included in the RCS portfolio.

  o **Research into the feasibility of implementing vector control where LF elimination with MDA alone by 2020 cannot be guaranteed.**

    ▪ **Context and rationale:** In 22 LF endemic districts, LF prevalence is still above the 1% threshold for stopping MDA despite 10 years of MDA. Recently LF clinical cases were identified in 11 districts previously considered not endemic, i.e. without MDA. In many countries, in particular in Africa, progress towards meeting health-related 2015 Millennium Development Goals (MDGs), the new Sustainable Development Goals (SDGs) and disease control/elimination targets is lagging. TDR is currently addressing the lack of research capacity among ministry of health (MOH) staff through the SORT IT and IMPACT grants. A complementary approach is the promotion of collaboration between MOH staff and national academic institution researchers.

    ▪ **IIR activities:** A pilot collaboration was established between Noguchi Memorial Institute (one of the institutions collaborating in the projects for the identification of genetic markers) and the Ghana Health Service. They are collecting epidemiological and entomological samples to assess the feasibility of using the methodology being developed for onchocerciasis (*O. volvulus*) xenomonitoring for LF.

    ▪ **Remaining challenges:** Review reports on experience with the collaboration from Noguchi Memorial Institute and Ghana Health Service with RCS for recommendation on whether and how to include such a research grant programme in the RCS portfolio. For genetic marker aspect, see above.

• **Malaria.** Strategies for surveillance/early detection of resistance in areas where Seasonal Malaria Control (SMC) is deployed. The objective of this project is to strengthen the evidence-base for guidance documents on drug surveillance in countries where SMC is deployed. The project is ongoing in Senegal and is conducted by the Department of Parasitology of the University of Cheikh Anta Diop (Prof. JL Ndiaye) and the National Malaria Programme of Senegal. The second population survey will be conducted in December 2015. Results and completion are expected Q2 2016.

  o **Remaining challenges:** Finalize the analyses and communicate the results for the benefit of other countries of the West African Region that will implement SMC in 2016.
Plans for 2016

- **Helminths:** All ongoing activities will continue into 2016-17 biennium. Based on discussion with the Scientific Working Group (SWG), all activities other than the 'Research for genetic markers of parasite response to the drugs controlling them' will be transitioned to Objective 4 of the 2016-17 workplan: Optimize Implementation of available interventions and strategies - Research in support of elimination programmes.

- **Malaria:** Publication of the results in an international journal (Q2/Q3 2016) and discussion of the results with the malaria control programmes implementing SMC during the next West Africa Rollback Malaria meeting (Q4 2016).

Objective 3: Strengthen evidence base

**EXPECTED RESULT 1.1.7 STRENGTHEN EVIDENCE-BASE FOR POLICY DECISIONS AND PROGRAMME IMPLEMENTATION BY MAXIMISING THE UTILITY OF AVAILABLE DATA (MERGED WITH 1.1.6 GAPS IN EVIDENCE THAT CAN BE REDRESSED BY HARMONIZING METHODOLOGIES, OR CAN BE ANSWERED BY OPTIMISING EXISTING DATA)**

**Context and rationale:** The evidence base for neglected tropical diseases and tropical diseases at large is often insufficient, weakening the strength of WHO recommendations on interventions. One of the problems sustaining this problem is methodological deficiencies in the trials which should inform decisions. This work combines systematic review and meta-analysis of aggregate data from publications with the creation of individual patient databases for more in-depth analysis, with the intention of deriving more comprehensive and robust information on the efficiency of interventions but also on essential questions on the methodologies underpinning these result.

Systematic reviews are considered the highest form of evidence that is used for instance to formulate WHO recommendations. The reality with infectious diseases of poverty is that, confident though we may be in the strength of this evidence, the amount of information that can be derived from this approach is limited by a number of methodological issues and their heterogeneity across trials. In this context, access to individual data and use of standardised methods would allow more in-depth analyses and strengthen the evidence-base. Ultimately, a collaborative approach to data collection and analysis is expected to bring up better solutions to alleviate the situation of the concerned populations, help control and eventually eliminate this disease.

**Progress in 2015**

All objectives have been achieved and additional activities have been added.

**Data-sharing platforms:**

- **Tuberculosis** drug trials. This is a joint initiative of three ‘data providers’ (TDR, TB Alliance, University of London) that sponsored three large trials on fluoroquinolone-based regimens (gatifloxacin, moxifloxacin); a fourth, Indian group has agree to join when their study is completed. Initial focus is on fluoroquinolones, to be expanded later. The hosting platform was selected through an open call. This is a ‘gated’ database with a Data Access Committee. The data-sharing agreement template, governance and technical issues regarding data cleaning and curation have been resolved; the three sponsors have now signed the data sharing agreement; and the three databases are now in the platform. The initiative was launched at the Union conference in Cape Town, December 2015 and the platform is expected to be accessible from March 2016.
- **Schistosomiasis** drug trials & control programme studies. This is a joint TDR - WHO/NTD initiative. A stakeholders meeting in September 2015 convened representatives of the research, control programme and donor communities. A systematic review identified potentially >20 000 participants who could contribute to the database (paper submitted). The meeting report has been posted on the TDR and NTD websites. A two-pronged approach was agreed: (i) dedicated databases (to address specific questions); and (ii) an overall schistosomiasis data-sharing initiative further development for 2016 to be discussed (see 2016 workplan). As for (i), initial 'collaborative' databases are already available (see below) or are in development (oxamniquine studies in Brazil with Fiocruz; praziquantel studies in S. japonicum with China CDC; praziquantel studies in preschool-aged children with NTD and investigators). There are prospects for extension to Soil-Transmitted Helminths (STH) (see 2016 workplan).

- **Cutaneous leishmaniasis** drug trials. Initial discussions have taken place between TDR and DNDi and stakeholders (redLEISH meeting, Medellin Colombia 1-3 July 2015).

- **Data management capacity.** Stakeholders in disease-endemic countries stressed the need to strengthen data management capacity – the curriculum is being developed (TDR IIR + RCS) in collaboration with Luxembourg Institute of Health and other partners.

**Remaining challenges:**

- Clearly define the role of TDR as the pathfinder and promoter of new initiatives but not a long-term funder. Projects should have a ‘business plan’ for sustainability.

- Communicate and disseminate. These principles should be communicated effectively in a publication which will lay out interim and long-term indicators to monitor outputs (what was achieved with different approaches), outcomes (how platforms are used), and impact (whether the quality of evidence increases and the rate at which information is gathered is accelerated).

- Ensure data quality and strengthen capacity for data management and meta-analysis in disease-endemic countries.

**Plans for 2016**

- Activate access to TB data-sharing platform and assess adequacy of governance, modus operandi, utility and promote the use of the platform.

- Progress development of schistosomiasis and cutaneous leishmaniasis data-sharing platforms involving stakeholders. Pilot specific databases to address control/research priority questions – e.g. oxamniquine in S mansoni; praziquantel in preschool-aged children.

- Advance development and test curriculum and training of data managers (see below.)

**Systematic reviews and meta-analyses of aggregated and individual participant-level data.**

- **Systematic review of the literature on vector control methods suitable for use in/around dwellings.** Vector control is an important means for reducing the prevalence of vector-borne diseases and resulting morbidity and mortality. Most reviews focus on single diseases or on the nature of the intervention. This review is a novelty because it focuses on the unit of allocation and will thus examine the utility of household/dwelling-based protection, 'delivered' through members of the household across diseases. This review was initiated in 2015. The first draft of the report/publication is expected for Q1 2016.
• **Schistosomiasis** treatment trials.
  
  o The above-mentioned initial 'collaborative' database of ~4700 patients (see 1.1.5) was analysed by comparing current and new methodological approaches (published: Olliaro et al, 2015\(^6\); data have been further modelled – paper submitted \(^7\)). This work aims at finding new, more reliable ways of expressing drug effects than current methods, which can be applied to schistosomiasis and STHs.

  o WHO is extending preventive chemotherapy with praziquantel to preschool-aged children and a new praziquantel paediatric formulation is being developed. However, little is known about the efficacy and safety of praziquantel in this age group. A systematic review of aggregated published data has been conducted (paper in preparation) to inform WHO recommendations and product R&D.

**Remaining challenges:** Work conducted in 2014-15 has shown the limitations of aggregated data meta-analyses when it comes to subgroups (age, dose): an individual participant database is under discussion for 2016.

• **Development of guidance on the use of modelling to support WHO guidelines.** Models are used to address different types of questions which are relevant to WHO guidelines when it is impossible or impractical to directly measure outcomes, either under experimental or natural conditions. TDR is funding a project implemented by the Secretariat of the WHO Guideline Review Committee to develop training and guidance for WHO staff on incorporation of the results of modelling studies in WHO guidelines.

**Remaining challenges:** This project was initiated in 2015. The results will be available and disseminated (e.g. via the WHO website) in 2016. TDR recognises that there are multiple players in this area. These players will then have a framework as to how guideline developers, policy-makers and modellers can engage and a better basis for understanding the rationale underlying WHO guidelines.

**Plans for 2016**

• **Schistosomiasis/STH.** Further explore and optimise analytical approaches of treatment outcomes to better understand inter-subject variability of response, and estimate better risk of suboptimal response/resistance which could affect control/elimination objectives.

**Research in support of TB control programmes in line with WHO/GTB endTB strategy**

This set of activities, which had originally been planned to start only in 2016 (as part of ‘Optimise Implementation of Available Interventions and Strategies’) was started earlier in 2015 after discussion with the SWG.

• **Tuberculosis operational and implementation research (OR/IR)**

  o **Context and rationale:** On 19 May 2014, the 67th World Health Assembly adopted the Global Tuberculosis Programme global strategy and targets for TB prevention, care and control after

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2015. There are 3 pillars in the strategy and one of them is “Intensified research and Innovation”. This project aims to support the pillar 3 of the EndTB strategy by exploring its implementation at the level of a region (instead of a country). We make the assumption that a regional dynamic will favour the design and conduct of OR/IR in the corresponding countries.

- **IIR activities**: The following activities were conducted:
  - With the support of TDR, the West African Regional Network for TB control (WARN-TB) was established in June 2015. It comprises the 16 countries of the West African region (Mauritania, Senegal, Cap Verde, Guinea Conakry, Guinea Bissau, Liberia, Sierra Leone, the Gambia, Mali, Burkina Faso, Ivory Coast, Ghana, Togo, Benin, Niger and Nigeria), has two co-chairs (Ghana and Guinea) and an executive secretariat based in Benin. The objectives of WARN-TB are to convene, coordinate, and facilitate communications between national programmes for TB control (NTPs), bilateral and multilateral organizations as well as private sector companies and civil society organizations; and promote OR/IR in NTPs and the efficient use of research outcomes to strengthen TB control within the West African Region. This was profiled in TDR news: West African regional network to develop national TB research agendas http://www.who.int/tdr/news/2015/west-african-regional-network/en/
  - TDR supported the WARN-TB countries in the development of their national TB research plan, with, (i) providing seed funds for launching the set-up of the national TB task force (multidisciplinary committee) in all countries in charge of developing the national TB research plan; and (ii) providing technical support for defining TB operational research priorities. In particular, a one-week workshop was organized in collaboration with WHO/GTB to strengthen the capacities and assist the national TB programmes of the WARN-TB in the analysis of their TB data, so that they can identify TB control gaps and priority areas for research including OR and IR. Some regional themes were identified.
  - TDR convened a meeting with the WARN-TB co-chairs, executive secretariat and academics/researchers for the North and the South in December 2015, to discuss specific training gaps for conducting TB OR/IR projects and for developing a two year training plan that combines already available training programmes (i.e. SORT IT, IR Tool Kit, massive open online course (MOOC) on IR, and all other courses developed by TDR or others as relevant). A “learn by doing” model with the mentoring of external tutors will be used. TDR supports the training and will provide small funding for conducting OR/IR that addresses research priorities as defined in their national research plan. Regional research themes are favoured.

**Remaining challenges:**

- Almost all countries need to set up their national TB task force led by the NTP, including national researchers, NGOs, civil society, etc. TDR will support finalising the development of the national TB research plan.
- There is an urgent need to strengthen the capacities of the TB surveillance system of the countries (e.g. rescuing and capturing in an adequate electronic format all historical data, harmonising data management tools and practices). This emerged as a key element for the countries to be able to define precisely their research priorities and for capturing the impact of the TB control strategies they will implement. TDR is seeking additional funding for 2016 to support these activities.
- The NTPs expressed training needs for strengthening their capacities for conducting OR/IR.
• The RAFAscreen project
  o **Context and rationale:** TB screening in high risk populations remains a challenge, and national tuberculosis programmes (NTPs) struggle to define adequate screening strategies adapted to their context and integrate new TB diagnostic tools such as GeneXpert.

  o **IIR activities:** The RAFAscreen project is an implementation research project conducted in collaboration with the national TB, HIV and non-communicable disease programmes of Benin, Guinea and Senegal for the rational use of TB diagnostic tools for the screening of TB in diabetic and HIV patients (high-risk for tuberculosis). This is a two-step project: a first phase is defining the more cost-effective screening strategy for the two patients’ types of each country; a second phase is implementation and assessment of acceptability/feasibility. The project started in October 2015 with the launch of the recruitment of patients in all three countries (9 000 patients will be screened in one year’s time). This project has leveraged €1.5 million over three years from the French government to the participating countries. TDR contributes to this project in terms of technical support for the coordination of the project (mentoring of the NTP of Benin) and the link with WHO/GTB. It was profiled in TDR news: Identifying effective screening strategies for tuberculosis among diabetic patients:


**Remaining challenges:** Provides technical support for the project management and the set-up of a phase 2-3 trial aiming at shortening multidrug-resistant tuberculosis (MDR TB) treatment to 6 months in Uzbekistan and Swaziland. This trial is sponsored by MSF (PRACTECAL Trial).

• **Research in support of malaria control/elimination**
  o **Context and rationale:** A planning meeting for operational research for malaria elimination was convened by the WHO’s Global Malaria Programme in Geneva, 17-18 October 2013. That meeting report listed operational research priorities in this field and recommended that TDR and GMP expand SORT IT used in Southern Africa to other groups of countries.

  o **IIR activities:** IIR contributed to:
    * a model to predict the effects on resistance of different ACT deployment strategies, which shows advantages of multiple first-line therapies (MFT; published Nguyen et al. 2015)
    * work investigating successful deployment and obstacles to rolling out the Test-and-Treat strategy (published Faust et al, 2015)
    * data to inform policy on dosing strategies for artesunate-amodiaquine
    * Support of the E8 Consortium on malaria elimination in Southern Africa. A SORT IT Phase 2 supported 12 operational research studies in the 4 eliminating countries (Botswana, Namibia, South Africa and Swaziland).

**Remaining challenges:** Securing funding for expansion of SORT IT activities in the malaria elimination field and developing a facilitator base with experience in malaria control/elimination.

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Plans for 2016

**PRACTICAL:** Continue to support ongoing activities in Uzbekistan and help set-up the project in Swaziland, including training of the MOH staff on drug development/regulation and GCP (at the request of the country MOH via WHO/GTB).

**RAFAscreen:** Phase 1 should end in Q3 2017.

**WARN-TB:** Start the delivery of the training plan developed. Research projects tackling national TB priorities will be developed as part of the training and small funding (US$ 10 000 to 20 000) will be provided to support the conduct of these OR/IR projects. Funding will also be sought for conducting OR/IR projects at the regional level. Based on the discussions that occurred during the previous WARN-TB meetings, a potential theme of research could be the implementation of new strategies for increasing TB case-finding. A common strategy that might be explored is to combine TB screening with other health programme activities such as the SMC campaign conducted by the malaria programme in almost all West African Countries. Another regional research theme could be to explore new strategies for increasing the use of TB diagnostics among children. Regional themes will be discussed with the WARN-TB and designated funds will be sought to support these regional TB research projects. Funds will also be sought for supporting WARN-TB activities. WAHO has already been approached and might be in a position to support the organization of the WARN-TB meetings. Further discussions will occur in 2016 for better articulating support from TDR and the West African Health Organization (WAHO).

**Data management capacity in countries.** Fully develop data manager curriculum and start training: one expressed training need of the NTPs is related to the data management for the “routine” programme activities but also for conducting research activities. A training programme will be developed in 2016 by a consultant and a group of experienced data managers from the TB programmes of the WARN-TB. This training will be piloted in 2016 and used in 2017 for other regions/programmes that express interest.

**DIAMA project:** *This is a new* European & Developing Countries Clinical Trials Partnership (EDCTP)-funded project (€3 million for 5 years) that was recently granted. This project aims at exploring new methods/tools for a “culture free” diagnostic and management of MDR-TB patients. TDR was involved in the development of the project that was submitted and will provide support for the project management, the set-up of the project and its conduct. The project will be conducted in Ethiopia, Benin, Senegal, Guinea (Conakry), Mali, Cameroon, RDC, Nigeria and Rwanda.

**EXPECTED RESULT 1.1.8: SAFETY DATA FOR POLICY DECISIONS**

This expected result has five projects.

1. **Piloting of pregnancy registry**

**Progress in 2015**

TDR participated in the WHO Global Malaria Programme’s (GMP) assessment of the safety of artemisinin derivatives when used in the first trimester of pregnancy in July 2015. In preparation for this meeting, the database from the pregnancy register protocol, which had collected data in Ghana, Kenya, Tanzania and Uganda, was analysed. A large number of datasets including a retrospective analysis of antenatal clinic (ANC) records of the Shoklo Malaria Research Unit (SMRU), Thailand; prospective observational studies in sub-Saharan Africa; and the pooled data from the pregnancy register protocol contributed to updated WHO recommendations on use of artemisinin-combination treatments (ACTs) in pregnancy undertaken by GMP. The key conclusions of the analysis were:

- Updated evidence on the safety of artemisinin indicates that ACT exposure in the first trimester of pregnancy does not increase the risk of miscarriage, stillbirths or major congenital malformations.
• Artemisinin exposure anytime during the first trimester has been associated with fewer miscarriages compared to exposure to quinine.

• Based on the available updated evidence, the first line treatment of uncomplicated malaria in the first trimester of pregnancy could be revised to include ACTs as a therapeutic option.

This activity has been completed (data to be published). Continued monitoring and pharmacovigilance of drug exposure in early pregnancy is needed.

2. Central database for pregnancy exposure registries

Context and rationale: In keeping with WHO’s recommendation that more data on the safety of treatment in pregnancy be prospectively collected, TDR is collaborating with WHO’s HIV department to support the development of a pregnancy drugs safety database to provide data on the proportion of cases of congenital anomalies diagnosed and linked to teratogenic exposures. The tool will help pool country data issued from national or local pregnancy exposure registries. This work is developed in collaboration with the HIV department, which recommends toxicity surveillance during pregnancy in the context of anti-retroviral use. It will also help collect data that may be relevant for other control programmes (e.g. malaria, tuberculosis) where important questions remain on the use of some drugs during pregnancy or during the first trimester of pregnancy.

Progress in 2015

A central registry for the collection and collation of data from pregnancy exposure registries and birth defects information was developed and is ready for piloting. An ad hoc working group has been organized to help finalize the discussion on key rules for the database and variables to be included. The discussion with countries and potential contributing sites have been initiated but no formal agreement has been reached yet (delay).

Remaining challenges: Commitments for contributing data (countries and/or research site) are not always easily obtained. IIR involvement will end in 2016-17 and discussions are being held with relevant WHO departments to take over, but sustainability in the long run has not yet been secured.

Plans for 2016

Advocacy for the pregnancy registry and training of interested sites is taking place, as well as continued collection, collation and analysis of data from contributing African centres where pregnancy registries are in place. A stakeholder meeting will take place in Q2 2016 and will bring together potential contributing sites and interested parties to discuss data sharing and work toward formalization of the agreements. A first full analysis of all the data collected by September 2016 is planned before the end of 2016.

3. Innovative approaches for safety monitoring at community level

Context and rationale: A major limitation of efforts to improve access to medicines and rapid scale-up to public health programmes is the lack of a monitoring programme of similar scale to assess potential safety issues. In many developing countries, safety monitoring systems are still weak, and under-reporting is a persistent problem. Numerous constraints and limitations may explain or contribute to this problem, and new approaches need to be identified in order to help countries and programmes have more efficient and reliable drug safety monitoring systems, in particular when preventive mass drug administration (MDA) programmes are in place and where drugs are administered at the community level and/or through community health workers to individuals who may or may not be infected with the pathogen in question. Traditionally, this applies to preventive chemotherapy (PC) programmes for helminthic diseases, but more recently this approach has been extended also to malaria, as seasonal malaria chemoprevention (SMC) in countries of highly seasonal malaria transmission.
Progress in 2015

Innovative approaches for safety monitoring are being tested in the context of mass drug administration.

- Following the workshop organized in October 2014 on innovative approaches for safety monitoring in the context of seasonal malaria chemoprevention (SMC), a study on safety monitoring, looking at the added value of m-health tools and benefit and feasibility of cohort event monitoring in the context of SMC, was conducted in Senegal. The data are currently being analysed.

- A call for applications for studies on PV in the context of MDA was published in March 2015, 27 applied, three were selected: Cameroon, Ghana and Tanzania, and protocols are being finalized. Also in the context of SMC, IIR is providing technical support for monitoring the safety of products delivered under SMC in countries involved in the UNITAID-funded ACCESS project, coordinated by the Malaria Consortium. One workshop was organized in Rabat, Morocco in collaboration with the Pharmacology Department (WHO Collaborative Centre) to strengthen the capacities of the national PV departments and the PV focal person of the malaria national programme of these countries. Progress was monitored during the course of 2015 SMC and will be assessed in 2016. This was profiled in TDR news: Strengthening safety surveillance in seasonal malaria chemoprevention campaigns in Africa: http://www.who.int/tdr/news/2015/safety_surv_mal_chemoprev_camp/en/

Remaining challenges: Implementation at larger scale of piloted approaches and sustainability of interventions.

Plans for 2016

- Analysis of the data obtained from the Senegal study on safety monitoring in SMC will be completed in 2016. Lessons learned will be shared with other SMC countries and discussion will take place to see if the strategies implemented could also be applied to other mass drug administration schemes.

- Study on PV in the context of MDA will be initiated in Cameroon, Ghana and Tanzania.

- A follow-up “lessons learned” meeting was organized in February 2016 to share experiences in safety monitoring during the 2015 campaign. The workshop brought together the different SMC implementing countries to review the performance of the PV system, identify areas that may need strengthening, identify further steps to improve the functioning of the system and disseminate and communicate results and lessons learnt.

- Consolidate evidence of drug safety for new drugs and regimens for treating multi-drug resistant tuberculosis (MDR-TB safety database). In collaboration with GTB, plans are being put in place to develop a central database for Serious Adverse Events (SAEs) for countries to comply with the obligation of having a system in place for active surveillance of MDR-TB drugs, a pre-requisite for the introduction of new drugs (currently bedaquiline and delamanid); this extends also to short treatments for MDR-TB: The concept note has been discussed and it is expected that a global central database could be ready for piloting in Q3 2016.

4. Optimize acquisition and analysis of safety data

Context and rationale: Quality-controlled collection, management and analysis of data is the backbone of evidence-based decisions. This need is particularly acute for safety data in disease-endemic countries. These projects fit well TDR’s dual role of promoting research to generate evidence for policies and of strengthening in-country capacities.
Progress in 2015

**Loa-loa in Gabon:** Support to the reference laboratory for the diagnosis of parasitic diseases in Gabon for capacity building on data management and data analysis of historical data. With technical assistance provided by LIH (Luxembourg Institute of Health) and IRD (Institut de Recherche pour le Développement), the centre will digitalise data from a cohort constituted of some 45 000 patients in areas co-endemic for loiasis, onchocerciasis and STH. Analysis will be carried out on the relationship between microfilaraemia, clinical symptoms of loiasis and treatment regimen with the objective to generate more evidence that will help understand, among other things, the relationship between microfilaraemia and tolerability (and efficacy), in order to establish the therapeutic window of treatment regimen. The capacity building activities and digitalisation of the records started in 2015. The data analysis should be possible by Q4 2016.

**Risk of anaemia following malaria treatment.** A dataset of nearly 9 000 patients treated with artemisinin combination therapies (ACT) and non-ACTs for falciparum malaria in Africa with haemoglobin records was compiled and analysed to unravel the risk of anaemia due to acute malaria and risks of anaemia caused by the treatment (adverse drug reaction) – Zwang et al, paper in preparation.

**Remaining challenges:** How to integrate information collected into decision-making for both research and control.

Plans for 2016

**Loa-loa in Gabon:** Upgrade data management system, analyse data and report results. Communicate results and promote policy uptake.

**Risk of anaemia following malaria treatment.** Finalize analyses and publish results.

5. **Capacity building for safety monitoring (UNDP Access and Delivery partnership project)**

**Context and rationale.** In many developing countries, safety monitoring systems are still weak, and under-reporting is a persistent problem. One of the main limitations is the lack of adequate training and awareness of health care providers. As a member of the UNDP Access and Delivery Partnership (ADP) project, TDR is involved in building capacity for pharmacovigilance in a selected number of countries (Ghana, Indonesia and Tanzania). The focus is on strengthening country capacity in five major areas. TDR is responsible for two of these areas - strengthening capacity of countries to monitor safety of new health technologies (implemented by IIR) and strengthening capacity to identify and address country-specific health system needs for effective access and delivery of new health technologies (implemented by RCS).

**Progress in 2015**

Different capacity building activities were organized or funded in Indonesia and Tanzania responding to a workplan prepared by the countries.

- **Indonesia:** Indonesia has been identified as one of the few pilot countries where bedaquiline will be introduced in the near future as part of a combination therapy of pulmonary tuberculosis due to multi-drug resistant strains of Mycobacterium tuberculosis (MDR-TB) in adults. In that context, the Indonesian Food and Drug Authority and Indonesia National TB Programme identified active safety monitoring as one of the key priority areas requiring capacity strengthening and support. A workshop on pharmacovigilance and introduction to cohort event monitoring was organized. The efforts toward building capacity for active safety surveillance will serve not only the introduction of bedaquiline but will give the country tools to ensure better safety monitoring of future drugs.
• Tanzania: The country prepared a 4-year workplan aimed at building further capacity on safety monitoring. Several “train-the-trainer” sessions to build capacity for safety monitoring among health care providers took place in 2015. They are expected to become trainers themselves, at the facility level and among other health care workers.

• Ghana: The focus has been on improving systems and piloting innovative approaches for safety monitoring at the community level. During Year 2, the Regional Centre developed a proposal to pilot the use of mobile technology for safety monitoring at the community level. The protocol for this pilot study is currently being finalized and the study will begin in Q3 2016.

Remaining challenges: Though needs are evident in all countries, it has taken some time to get the right people engaged in the countries and for them to dedicate time to the project.

Plans for 2016

Funding continues until March 2018. Capacity building activities will continue based on the annual renewed workplan for the project and the needs from each country. The workplan for the next 2 years is being discussed with the countries.

Objective 4: Optimize implementation of available interventions

This objective has five expected results.

EXPECTED RESULT 1.1.1: SUPPORT ADEQUATE COUNTRY RESPONSE TO EPIDEMIC CHALLENGES: EVIDENCE-BASED GUIDANCE FOR DENGUE OUTBREAK DETECTION AND RESPONSE

Context and rationale: In view of the enormous social and economic burden of dengue outbreaks, TDR coordinates research on strengths, limitations and options for improvement related to dengue surveillance, outbreak preparedness, detection and response in order to develop an evidence-based model contingency plan adaptable to country needs which will help to optimise country preparedness and response to dengue outbreaks. Working closely with the WHO/NTD Department, TDR is active in informing and mobilizing major stakeholders such as national control programmes and international organizations (WHO Regional Offices, International Red Cross Red Crescent, and others) in order to translate research findings – after completing the analysis and drafting a “model contingency plan” – into policy and practice.

Summary of past activities and achievement: This project is conducted in partnership with a number of research institutions and national control programmes of dengue endemic countries in Latin America and Asia (IDAMS, an EC FP7 project). Interviews on dengue surveillance and outbreak detection and response were conducted in 10 Asian and Latin American countries, and a comparative analysis of outbreak response plans in 14 countries was published. Additionally, systematic literature reviews on dengue surveillance and outbreak response were published, which included cost assessments on the use of the revised dengue case classification and the effectiveness of different vector control interventions. Based on these analyses, (1) a study on the sensitivity and predictive value of a number of candidate alarm signals for dengue outbreaks was completed using 5 to 10 years of retrospective data in 5 countries; and (2) a model contingency plan was drafted, with agreed outbreak definitions and country-specific risk assessment schemes, to initiate early response activities according to the outbreak phase. This would also allow greater cross-country sharing of ideas.
Progress in 2015

The analysis of the retrospective study on alarm signals for dengue outbreaks in 5 countries (Brazil, Mexico, Dominican Republic, Malaysia and Viet Nam) and the first experiences with the prospective study led to the following conclusions, which were developed during an international expert meeting: (1) Calculations of alarm indicators predicting dengue outbreaks showed both sensitivity and positive predictive value to be between 80-90%. The signals vary among and even within countries and require additional effort to train country teams to identify their specific signals (paper submitted); (2) Preliminary prospective country reports show active data capture and improved in-country capacity for predictive dengue outbreak assessments; (3) A dengue risk framework is proposed for further testing using a traffic light system and/or scoring system that encompasses qualitative and quantitative risk indicators for dengue outbreaks to allow countries to move from one alert level to another; (4) Preliminary cost-effectiveness modelling shows the potential break point when early warning and response are not cost-effective.

Remaining challenges: Updated datasets need to be analysed to further stabilise correlations between alarm and outbreak indicators; and new analyses have to be done on additional indicators, such as the NS-1 positivity rate and notified cases. After completing the project, results need to be disseminated and policy uptake promoted throughout WHO and the countries. Further applicability of approaches identified through this project need to be identified in a broader range of countries and beyond dengue (other Aedes-borne arboviruses can coexist such as chikungunya and Zika, which are flagged as priority diseases of epidemic potential by the WHO R&D Blueprint).

Plans for 2016

Completion of current activities:

- The prospective study will be completed in October 2016 and subsequently analysed (a first draft report is expected by the end of the year).
- The above mentioned workbook (“model contingency plan”) will be complemented with the results of the prospective study and tested in a number of dengue endemic countries.
- The final meeting of the IDAMS network (WPS) will be organized in June in Geneva where the results of the different work packages on clinical warning signs for severe dengue, basic research on the dengue virus and diagnostics, measuring the burden of dengue and the above presented dengue outbreak research, will be presented and discussed.

New activities:

- Exploration of how TDR can be better adapted to help countries prepare and respond to epidemic challenges. Develop a plan to expand and adapt approaches to include the range of vector-born viral infections caused by arboviruses (dengue, Chikungunya and Zika because they are carried by the same vector) with a focus on urban settings, where these outbreaks tend to occur. Urban health is an area of work for VES, and together we will develop an approach (based on prior achievements) which will also include social, economic and environmental determinants, as well as the involvement of civil society and communities. This will also be part of the response to the WHO Blueprint.
- A close collaboration between IIR and VES is being established where the IIR findings on outbreak detection and response will be made available and used by the Caribbean Network established by VES, and the findings from novel dengue vector control methods in urban settings developed in the VES programme will be made available to the counties and teams working on dengue outbreak management.
EXPECTED RESULT 1.2.1: INTERVENTION AND IMPLEMENTATION RESEARCH TO INFORM POLICIES FOR THE ELIMINATION OF VISCERAL LEISHMANIASIS (VL) IN THE INDIAN SUBCONTINENT (BANGLADESH, INDIA AND NEPAL)

Context and rationale: Since 2005 TDR has been working with both research and control in the Indian subcontinent countries (ISC) to conduct research that informs policy and practice in the region to achieve the elimination target of 1 VL case per 10 000 inhabitants. These efforts represent one of the longest and most successful implementation research programmes at TDR that have contributed to a sharp reduction of VL/PKDL cases in the ISC. Studies have been conducted on patients’ health seeking behaviour—particularly the delay in seeking care—on active case detection of VL/PKDL (Post Kala-azar Dermal Leishmaniasis). Different approaches have been used, such as house-to-house screening, fever camps, contact tracing around index cases, and village health worker approach. Studies have included improved treatment strategies, the operational feasibility of novel IV drugs, improved tools for vector control and strategies for monitoring national IRS (indoor residual spray) programmes and the specific challenges of PKDL detection and treatment. The attack phase of the project is completed with the exception of some pockets in India and fewer in Bangladesh. The elimination target objective is within reach. However, fewer cases means that the strategy must be adapted, and the consolidation and maintenance phase require different approaches. This area of work now combines the three main components which are key at this stage of the VL elimination campaign: (1) active case detection; (2) vector control and reduction of transmission; and (3) research policy interface.

Progress in 2015

All objectives were met and activities are on track. Additional projects were conducted.

Projects completed: During 2015 the study on the combined approach of active case detection (VL/PKDL, leprosy, TB, malaria together with VL vector control through bed net impregnation) was completed and published 11. The study on treatment and reporting delays of VL cases was also published 12. The cluster randomized trial on various vector control interventions was analysed (showing that Durable Wall Lining (DWL) had the highest and longest impact on VL vector densities) and was submitted for publication 13. An additional study on covering only parts of the walls with DWL showed promising results on cost reductions and will be published soon14. A review of the VL vector characteristics to adapt national control programmes has also been submitted. 15

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15 Rajib Chowdhury, Vijay Kumar, Dinesh Mondal, Murari Lal Das, Aditya Prasad Dash, Axel Kroeger. Implication of vector characteristics of Phlebotomus argentipes in the Kala-azar elimination programme in the Indian subcontinent (submitted)
Projects started: Two studies were planned in 2014 with the respective country control programmes and researchers in Nepal and Bangladesh to test effective, sustainable interventions to detect cases and halt transmission in areas of low VL prevalence where the 1 case in 10 000 population target is being achieved. During 2015 the study protocols were finalised and approvals obtained from local ethics committees, regulatory authorities and the WHO Ethics Review Committee, the latest granted in August 2015. Delays were mainly due to the earthquake in Nepal which interrupted all activities for almost 3 months. An additional practical hurdle was that arrangements for shipping and allowing the importation of the study materials (durable wall lining for the study in Bangladesh, and insecticidal paint for the study both in Bangladesh and Nepal) were to be made; they are now available in the countries. In both countries training materials, including Standing Operating Procedures (SOPs) for installing the durable wall lining and the application of the paint, have been developed and validated in the field. Whilst the current project has started in Bangladesh, the initiation of the field study in Nepal has experienced additional delays due to the political instability in the study area. However, activities related to objective 1 of the project (review and assess current active case detection, vector control and reporting methods) could be initiated in both countries, and the testing of sand flies for insecticide resistance are commencing.

The annual meeting of TDR supported VL research, which brings together national programme managers, researchers and international experts, was held in November 2015. Eight topic areas were reviewed: (1) Research on new emerging VL foci in Bangladesh and Nepal; (2) The need for improved communication and information exchange systems in remote areas of Nepal and Bangladesh; (3) Genetic diversity of parasites in Nepal and Bangladesh; (4) Feasibility of point-of-care molecular diagnosis (PCMD) of VL and other febrile diseases; (5) PKDL challenge; (6) Assessment of unregistered cases to determine the unreported case load (as a precondition for certification of elimination by WHO South-East Asia Regional Office); (7) Vector bionomics including behaviour and alternate vector control tools; (8) Uncertain efficacy of locally produced VL drugs in Bangladesh. When discussing the priority research areas, the meeting participants recommended conducting studies to determine the extent of the new emerging VL foci as well as possible sources of infection, including examination of local sand flies for parasite infection. Bangladesh and Nepal acknowledged the need to implement research programmes to follow up on asymptomatic cases and on the infection potential of PKDL. Currently a TDR-commissioned systematic literature review is looking at the published evidence; it will be followed by an expert meeting in Kathmandu in March 2016. Other recommendations included continuing the current TDR-supported studies on improved vector management – analysing the effect of controlling the vector through insecticidal paint or partial durable wall linings, and including communities and village health workers in the control – and active VL case detection for the last push towards elimination and the continued effort during the consolidation and maintenance phase.

Other activities: There is a close interaction with WHO’s Neglected Tropical Disease department and non-state actors. We contributed to the kala-azar elimination programme (KEP) meeting in February 2015 and, in response to questions raised at the meeting on the need for modelling the impact of interventions, participated in a study of health-seeking, diagnostics and transmission

Remaining challenges: As the elimination target of 1 VL case in 10 000 population is being achieved, countries are facing the problem of how it can be maintained, which interventions are sustainable, and how to prevent future resurgence. This also means achieving a better understanding of transmission dynamics.

Plans for 2016

The implementation research studies described above will be continued and the final results are expected by the end of 2016. The development of new research proposals outlined at the expert meeting in November 2015 (see above) will be discussed in the forthcoming Kathmandu meeting on the VL transmission potential of asymptomatic and PKDL cases as well as on the relapse rate of treated/untreated VL cases. The proposals will then be translated into research protocols which will be implemented, after ethical clearance, in 2017.

Other critical questions are: how will elimination of the disease (as a public health problem, not elimination of the infection) be certified? What are the practical consequences? How can this be done with imperfect diagnostics? How will achievements be sustained when the interventions are removed? What does 1/10 000 mean in terms of the basic reproduction rate? What is the reservoir (role of asymptomatic infections, PKDL in perpetuating transmission)?

EXPECTED RESULT 1.2.2: COMMUNITY-BASED SCHEDULED SCREENING AND TREATMENT OF MALARIA IN PREGNANCY FOR IMPROVED MATERNAL AND INFANT HEALTH (COSMIC)

Context and rationale: The overall objective of TDR’s role in this multi-country study is to create “policy panels” that bring together policy-makers, healthcare providers, researchers and the press to learn and contribute to this study. The goal is to securing commitment so that, if the results are favourable, the necessary policy and practice changes can be implemented as soon as possible. TDR is doing this as part of efforts to explore effective methods for supporting the transfer of research results to policy and practice improvements. Consequently, this project fits within not only research, but also knowledge management.

Progress in 2015

One of the recommendations that came out of the original policy panel meetings was to provide updates on the progress of the research and any issues that came up, which was done in March and April of 2015. Planning for the final policy panel meetings (scheduled for August, 2016) has begun. Site visits were conducted at each of the 3 sites (Benin, Burkina Faso and the Gambia) in November and December to record photos and videos that can be shared at the final policy panel meetings. The objective of this is to provide the panel members with the perspective of those in the field who may not be able to attend the final policy panel, and to use appropriate methodology to share qualitative data through interviews and imagery.

Remaining challenges: The Benin site was not able to recruit enough women to the study because of fears that the study and placental biopsies were related to an infant death. This has led to examining how to better manage misunderstandings early in the communities. COSMIC is studying scheduled screening and treatment by community healthcare workers in communities as an adjunct to IPTp, so it is unknown whether a new WHO policy against intermittent screening and testing at antenatal clinics will confuse or negatively affect perceptions among policy-makers. The issue beyond this project remains – how to increase the percentage of pregnant women who receive both preventive care and treatment as needed. This study is one approach that will need to be studied in context with other analyses on how to increase access and identify effective alternative delivery approaches.

Plans for 2016

The research consortium has requested a no-cost extension of 6 months for the scientific work and an additional 3 months for dissemination activities (the TDR policy panels) and management (final report). If agreed, this would postpone TDR 2016 planned work to conduct final policy panels in each of the 3 countries to early 2017, with project closure in May 2017.
EXPECTED RESULT 1.2.3: IMPROVED MANAGEMENT OF CHILDHOOD FEBRILE ILLNESSES

Context and rationale: Data on the pathogens causing infection in babies born at home are scarce, particularly for infections in the first weeks and months of life. These data are necessary to provide insights on the antibiotic regimens that can be used in case management for serious infection in young infants in out-patient or home settings in developing countries and are particularly valuable in areas of high neonatal mortality, using explicitly defined criteria for community acquired infections. Following a recommendation from the 2014 February meeting of the ad-hoc Scientific Advisory Group, TDR’s focus was redirected to severe infection in young infants. Though there is a growing interest for this field of research, most groups usually target children between 2 months and 5 years, but exclude very young infants, particularly in African settings. TDR is one of the few groups working on severe infections in very young infants (0-2 months).

Progress in 2015

In keeping with the above-mentioned recommendations, this project focuses on the microbiological causes of invasive infections in young infants (0-2 months) in rural African settings.

- **Prospective study.** The master protocol has been finalized, and two sites were selected (one in Tanzania and one in Burkina Faso) for the conduct of the study. The site specific protocol was submitted to the local Ethics Committee (EC) and the study prepared.

- **Retrospective study.** In parallel, a specific call for secondary complementary analysis of retrospective data and samples was issued in August and a site in Kenya selected. The study considers the additional analysis of left-over blood samples by molecular biology techniques (TaqMan arrays card) in order to try to identify pathogens which would have been missed by conventional haemoculture. The site specific protocol was submitted to the local Ethics Committee (EC) and the study prepared.

Remaining challenges: Implementation is delayed. Activities have been slow to start due to a combination of delays at different levels: delay in review of the application submitted, delay in submission and approvals to the ERC. Due to the low yield and sensitivity of the haemoculture, it may be difficult to draw representative conclusions from the study.

Plans for 2016

The prospective study is expected to be completed by Q4 2016 or Q1 2017 in Burkina and Q1/Q2 2017 in Tanzania. Full data analysis should be completed by end of 2017. The retrospective study should be completed in 2016 and final data analysis ready in 2017.

EXPECTED RESULT 1.2.4: STRUCTURED OPERATIONAL/IMPLEMENTATION RESEARCH AND TRAINING INITIATIVE (SORT IT)

Context and rationale: Since 2012, TDR has led the Structured Operational research and Training Initiative (SORT IT). SORT IT aims to support countries to:

a) Conduct operational research around their own priorities;

b) Build adequate and sustainable operational research capacity within their public health programmes;

c) Create an organizational culture where operational research continually informs improvements in public health programme performance and ultimately public health.

SORT IT activities currently take two forms: stand-alone courses and programmes comprising eight phases of activity over a 3-4 year period, of which the second phase is the SORT IT course.
The eight phases are:

**Phase 1:** Dialogue with ministries of health and targeted public health programmes to determine the country’s priorities for OR/IR and its capacity-building needs. This phase is conducted through TDR and the WHO infrastructure at headquarters, regional and country offices. It facilitates the translation of research findings into policy and practice at a later stage.

**Phase 2:** TDR and the WHO offices at regional and country level engage with a host institution in-country to organize an integrated operational research and training course. This involves three workshops and mentoring over the course of one year to take a research project from proposal writing to publication of a research paper. The goal is to have research papers produced out of this work published in open-access journals and in the most appropriate languages for effective dissemination of the results.

**Phase 3:** TDR and WHO organize a number of follow-up activities to further disseminate the research findings and provide further training for SORT IT participants. This includes the organization of a symposium around a relevant international or regional conference. Participants are also encouraged to present their work at national and regional meetings, including WHO meetings.

**Phase 4:** TDR and WHO organize a four-day workshop on translating research into policy and practice. This is conducted in collaboration with EVIPNet (the Evidence into Policy Network) hosted by WHO. SORT IT participants are introduced to the process of research translation and supported to develop ‘evidence briefs for policy’ (EBPs) from their published research paper.

**Phase 5:** Research papers from Phase 2 and the EBPs are presented to national authorities. The WHO regional and country offices work to ensure that there is a formal consideration of the implications of the SORT IT research for policy and practice and also for future research. TDR and WHO formally follow-up on the impact of SORT IT research on policy and practice one year after presentation of the EBPs to national authorities.

**Phase 6:** Once the policy and practice implications of completed research have been considered, countries are encouraged to consider what further research is needed and capacity building is required. This forms the basis of a second SORT IT cycle (Phases 1 - 8). The use of new or existing TDR award grants (such as the TDR regional small grants) support SORT IT alumni to continue their research activities.

**Phase 7:** Operational/implementation research fellowships allow SORT IT alumni to remain active in operational research within their public health programme. Designated funding is being sought for this. An OR/IR fellowship could be a key component of leadership development and would need to be developed in partnership with the ministry of health and take into consideration the broader national strategic plans.

**Phase 8:** Assessment of the SORT IT programme and its contribution to research, capacity building and impact on policy and practice.

Since 2012 the initiative has:

- Increased the number of research projects and people trained
- Broadened the range of public health issues addressed in SORT IT
- Increased the complexity of research undertaken
- Expanded the partnership base
- Enhanced the potential for SORT IT research to influence policy and practice

The initiative is moving from international courses based in Western Europe to more sub-regional and national activities, and from courses to SORT IT programmes. SORT IT activities are now being conducted in English, Russian and Spanish. SORT IT training materials are currently being translated into Portuguese by PAHO. Efforts are under way to develop a French-language SORT IT Programme in Guinea.
Thirteen sub-regional or national SORT IT programmes are under way. One sub-regional programme (Eastern Europe) started in 2013, and two sub-regional programmes (Central Asia and Latin America/Caribbean) started in 2014. SORT IT partners (particularly the Union and MSF) completed 10 stand-alone OR courses during the biennium with TDR support.

**Progress in 2015**

One sub-regional programme (Southern Africa) and 9 national SORT IT programmes started in 2015. Activities are indicated in the table below.

A major development in 2015 is the launch of two national programmes led and conducted entirely by public health workers in the country or neighbouring countries. Most of these workers have been trained in OR and mentored as facilitators through SORT IT.

TDR also supported two, one-day operational research skills workshops in 2015: one in Sydney during the Union Western Pacific Regional Conference and one in Cape Town at the World Lung Health Conference. The latter had more than 140 registered participants.

Much effort has been made to take operational research beyond published papers. TDR partners with the WHO Evidence-Informed Policy Network (EVIPNet) on Phases 4 and 5 of SORT IT Programmes. In August 2015, 24 SORT IT facilitators completed an “Evidence-Informed Policymaking (EIP) - Training of Trainers Workshop”, funded by TDR and supported by EVIPNet and the WHO European Regional Office (EURO). The workshop was hosted and led by the Uganda National EVIPNet Unit at the College of Health Sciences, Makerere University, Kampala. The EVIPNet Evidence-Informed Policy-making process involves two steps: a) development of an evidence brief for policy; and b) a policy dialogue. An outcome of the Training of Trainers Workshop was that most SORT IT facilitators felt that the transition from OR training to developing an evidence brief for policy would be too difficult for the majority of SORT IT trainees. TDR and EVIPNet have developed an intermediate step – the development of Issue Briefs for Policy (IBP). Training materials and a workshop format were developed for this and the first workshop was held in Riga, Latvia, in December 2015. Trainees of the Eastern Europe Programme were supported to develop IBPs from their SORT IT research papers.

TDR and the Gates Foundation began supporting WHO EURO and the Global TB Programme in 2015 to develop the SORT IT Network in Eastern Europe and Central Asia into a data-sharing platform that could support research related to MDR and XDR-TB control across countries. A training workshop on data-sharing and analysis is being developed in partnership with the Liverpool School of Tropical Medicine and the College of Health Sciences, Makerere University, Uganda. The first training workshop will be held in Istanbul in February 2016. It is expected that the immediate focus of data-sharing research done by these countries will be the safety of new drugs for MDR TB.

In late 2015, TDR and the Union obtained funding from DFID to run SORT IT Programmes in two of the countries worst affected by the Ebola Virus Disease (EVD) Outbreak: Liberia and Sierra Leone. TDR will support a third programme in Guinea. These programmes will be a proof-of-principle test if SORT IT can be used to help the rapid and evidence-informed recovery of health systems after humanitarian disasters such as the EVD Outbreak. The ministries of health in all three countries consider the SORT IT Programmes to be part of the national health systems recovery plans. The subjects for research will be broad – including EVD survivor care, malaria, TB, HIV, NTDs, nutrition, immunization, etc. In line with the national priorities for health systems recovery, the capacity-building will focus on the district level and the strengthening of district health management teams. WHO Country Offices in all three countries are enthusiastic partners. Phase 1s have been completed in each country.
<table>
<thead>
<tr>
<th>Country/sub-region</th>
<th>RO</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Phase 4</th>
<th>Phase 5</th>
<th>Phase 6</th>
<th>Phase 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. Europe</td>
<td>EURO</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>C. Asia</td>
<td>EURO</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Latin America and Caribbean</td>
<td>PAHO</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Southern Africa</td>
<td>AFRO</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
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<td>X</td>
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<td></td>
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<tr>
<td>Peru</td>
<td>PAHO</td>
<td>X</td>
<td>X</td>
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<td></td>
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<td></td>
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<tr>
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<td>EURO</td>
<td>X</td>
<td>X</td>
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<td></td>
<td></td>
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<td></td>
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</tr>
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<td>Sierra Leone</td>
<td>AFRO</td>
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<td>made</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liberia</td>
<td>AFRO</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Guinea</td>
<td>AFRO</td>
<td>X</td>
<td>Jan 16</td>
<td></td>
<td></td>
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<tr>
<td>Colombia</td>
<td>PAHO</td>
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<td></td>
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<tr>
<td>Suriname</td>
<td>PAHO</td>
<td>X</td>
<td>Q1 2016</td>
<td></td>
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</tr>
</tbody>
</table>

**Remaining challenges:** Availability of SORT IT facilitators remains the single biggest challenge to expansion. Regional pools of facilitators for all SORT IT phases need to be developed in order to support the start-up of national programmes. As national programmes are started, there must be plans to ensure a sustainable critical mass of facilitators at national level. Such national capacity can also contribute to SORT IT activities elsewhere in their region and support other countries to start national programmes.

**Plans for 2016**

Plans include completion of SORT IT programmes already started and ensuring that all programmes that have been started benefit from the 8 phases of a SORT IT Programme. Where SORT IT Programmes have been successfully implemented, advocacy is needed that will lead to the uptake of programmes in other countries and the repeating of SORT IT Programme cycles in those countries that have already implemented.

Phases 1 to 3 need to be transitioned into other UN languages and will follow the successful model it developed for Russian and Spanish. The development of a French language SORT IT Programme and translation of materials will be conducted in the context of the Guinea SORT IT Programme. The transition of SORT IT into Portuguese could be effected through a SORT IT Programme in the non-eliminating countries of the E8 Consortium (specifically Angola and Mozambique) and funding will be sought for this.

Phase 2 workshops will start 11 January 2016 in Sierra Leone and 18 January in Liberia. Phase 1 completed in Guinea, Phase 2 subject to availability of funds. The usual 10-month timeframe of Phase 2 is being shortened to 7 months in these programmes, with preliminary research findings available to the ministries of health within 4 months of starting the research. This is ambitious but necessary to inform health systems development in a timely manner.
Phases 4 and 5 (the evidence-informed policy phases) will be further developed and Phases 6 and 7 (the consolidation and leadership development phases) strengthened. This will be done in partnership with EVIPNet and with TDR colleagues in the Research Capacity Strengthening and Knowledge Management Unit.

In 2016, TDR needs to identify reliable and substantial funding sources to drive the uptake and implementation of SORT IT by countries. In 2017, TDR will implement its first SORT IT Phase 8: the independent evaluation of the impact of the SORT IT Programme in Eastern Europe.

NEW EXPECTED RESULT FOR 2016-17 BIENNium: TRANSLATING NEW AND TRADITIONAL KNOWLEDGE INTO HEALTHY ENVIRONMENTALLY SUSTAINABLE HOUSING

This project (discussed at the previous SWG meeting) will be initiated only if designated funding can be raised. Fund raising activities are planned for 2016, with, in case of success, project initiation only in 2017.
### 8. 2014-15 financial implementation

#### IIR Expected results

<table>
<thead>
<tr>
<th>Operation Activities IIR</th>
<th>2014-15 implementation</th>
<th>TOTAL</th>
<th>UD</th>
<th>DF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response to dengue outbreaks</td>
<td>Approved budget ($60m)</td>
<td>Approved revised planned costs (Oct-14)</td>
<td>Implementation at 31 Dec 2015 (Exp + Enc)</td>
<td>Implementation rate against planned costs</td>
</tr>
<tr>
<td>Critical gaps hindering control programme objectives: vulnerability to resistance</td>
<td>1.1.1</td>
<td>500,000</td>
<td>900,000</td>
<td>1,260,000</td>
</tr>
<tr>
<td>Facilitate innovation to generate tools to achieve control programme objectives</td>
<td>1.1.4</td>
<td>1,540,000</td>
<td>1,518,689</td>
<td>1,490,527</td>
</tr>
<tr>
<td>Consolidating and presenting the evidence platform necessary for WHO recommendations</td>
<td>1.1.5</td>
<td>400,000</td>
<td>624,444</td>
<td>634,579</td>
</tr>
<tr>
<td>Safety data for policy decision</td>
<td>1.1.6</td>
<td>1,170,000</td>
<td>1,630,000</td>
<td>1,940,527</td>
</tr>
<tr>
<td>Research to inform policies for the elimination of Visceral Leishmaniasis (VL) in the Indian Sub-Continent (ISC)</td>
<td>1.2.1</td>
<td>1,155,000</td>
<td>1,518,689</td>
<td>1,518,689</td>
</tr>
<tr>
<td>Community-based scheduled screening and treatment of malaria in pregnancy for improved maternal and infant health: a cluster-randomized trial</td>
<td>1.2.2</td>
<td>58,000</td>
<td>58,550</td>
<td>58,550</td>
</tr>
<tr>
<td>Improved management of childhood febrile illnesses</td>
<td>1.2.3</td>
<td>2,400,000</td>
<td>650,000</td>
<td>650,000</td>
</tr>
<tr>
<td>Structured Operational / Implementation Research and Training Initiative (SORT-IT)</td>
<td>1.2.4</td>
<td>3,737,000</td>
<td>1,856,530</td>
<td>1,435,590</td>
</tr>
<tr>
<td>IIR Operations</td>
<td>11,710,000</td>
<td>8,445,752</td>
<td>7,604,450</td>
<td>90%</td>
</tr>
</tbody>
</table>

#### Strategic Development Fund (SDF) Expected results

<table>
<thead>
<tr>
<th>Operation Activities SDF</th>
<th>2014-15 implementation</th>
<th>TOTAL</th>
<th>UD</th>
<th>DF</th>
</tr>
</thead>
<tbody>
<tr>
<td>VES Activity</td>
<td>Approved budget ($60m)</td>
<td>Approved revised planned costs (Oct-14)</td>
<td>Implementation at 31 Dec 2015 (Exp + Enc)</td>
<td>Implementation rate against planned costs</td>
</tr>
<tr>
<td>IR Activity</td>
<td>3</td>
<td>0</td>
<td>800,000</td>
<td>627,304</td>
</tr>
<tr>
<td>RCS Activity</td>
<td>3</td>
<td>0</td>
<td>403,383</td>
<td>300,633</td>
</tr>
<tr>
<td>One TDR Activity</td>
<td>3</td>
<td>0</td>
<td>951,621</td>
<td>958,090</td>
</tr>
<tr>
<td>SDF Operations</td>
<td>2,720,000</td>
<td>2,740,004</td>
<td>2,294,831</td>
<td>84%</td>
</tr>
</tbody>
</table>
9. 2016-17 revised planned costs

- In January 2016, one of TDR’s major donors announced that their contribution to development programmes would decrease by 30% to address the current immigration situation. Anticipating a possible decrease from other donors, TDR cautiously decided to revise its income forecast accordingly with a reduction of US$ 5 million undesignated funds (from US$ 35 million to US$ 30 million).
- As salaries and operational costs are fixed costs, the reduction of US$ 5 million undesignated funds has been implemented across the operations planned costs. Contingency revised planned costs have been developed reflecting a decrease of 30% of the operation budget undesignated funding of US$ 45 million budget scenario planned costs (from US$ 16.1 million to US$ 11.1 million).
- This led to a decrease of (i) US$ 1.2 million of the strategic development fund planned costs (no new projects until new funds become available); (ii) US$ 0.9 million for the planned costs of the Implementation and Intervention Research area; (iii) US$ 0.6 million for the planned costs of the research for Vector and Environment and Society area; and (iv) US$ 2.2 million of the Research Capacity Strengthening and Knowledge Management area planned costs.
- Balance of funds unspent in 2014-2015 has been carried over to 2016-2017 and delayed activities will be implemented against it.

<table>
<thead>
<tr>
<th>Intervention and Implementation Research (IIR)</th>
<th>$45M Scenario</th>
<th>$40M reduced plan</th>
<th>2014-15 commitments</th>
<th>Revised planned costs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DF</td>
<td>UD</td>
<td>UD reduction</td>
<td>revised UD</td>
</tr>
<tr>
<td>Facilitate Innovation</td>
<td>-</td>
<td>205,000</td>
<td>(50,000)</td>
<td>155,000</td>
</tr>
<tr>
<td>Sustain intervention effectiveness</td>
<td>-</td>
<td>575,000</td>
<td>(26,000)</td>
<td>549,000</td>
</tr>
<tr>
<td>Vulnerability of chemotherapy for helminths to resistance</td>
<td>-</td>
<td>560,000</td>
<td>(11,000)</td>
<td>549,000</td>
</tr>
<tr>
<td>Enhance surveillance for malaria drug resistance</td>
<td>15,000</td>
<td>15,000</td>
<td>15,000</td>
<td>15,000</td>
</tr>
<tr>
<td>Strengthen evidence base for WHO recommendations and Country policies</td>
<td>720,000</td>
<td>540,000</td>
<td>(140,000)</td>
<td>400,000</td>
</tr>
<tr>
<td>Maximize use of available data for policy decisions</td>
<td>300,000</td>
<td>300,000</td>
<td>(85,000)</td>
<td>215,000</td>
</tr>
<tr>
<td>Optimize acquisition and analysis of new safety data for policy decisions</td>
<td>720,000</td>
<td>240,000</td>
<td>(55,000)</td>
<td>185,000</td>
</tr>
<tr>
<td>Optimize interventions in support of control programmes</td>
<td>1,680,000</td>
<td>2,280,000</td>
<td>(684,000)</td>
<td>1,596,000</td>
</tr>
<tr>
<td>Structured Operational Research and Training Initiative (SORT IT)</td>
<td>1,000,000</td>
<td>700,000</td>
<td>(250,000)</td>
<td>450,000</td>
</tr>
<tr>
<td>Strategies to accelerate research to policy translation (COSMIC)</td>
<td>40,000</td>
<td>40,000</td>
<td>40,000</td>
<td>40,000</td>
</tr>
<tr>
<td>Research on Dengue outbreak response</td>
<td>160,000</td>
<td>250,000</td>
<td>(45,000)</td>
<td>205,000</td>
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<tr>
<td>Research on elimination of VL in the Indian Sub-Continent</td>
<td>150,000</td>
<td>500,000</td>
<td>(111,000)</td>
<td>389,000</td>
</tr>
<tr>
<td>Research on management of febrile illnesses</td>
<td>-</td>
<td>30,000</td>
<td>-</td>
<td>30,000</td>
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<tr>
<td>Translating knowledge for healthy housing</td>
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<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Research on improved TB control</td>
<td>330,000</td>
<td>800,000</td>
<td>(278,000)</td>
<td>522,000</td>
</tr>
<tr>
<td></td>
<td>$45M Scenario</td>
<td>$40M reduced plan</td>
<td>2014-15 commitments</td>
<td>Revised planned costs</td>
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<td>----------------------</td>
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<tr>
<td></td>
<td>DF</td>
<td>UD</td>
<td>UD reduction</td>
<td>revised UD</td>
</tr>
<tr>
<td>Strategic Development Fund (SDF)</td>
<td>-</td>
<td>1,150,000</td>
<td>(1,150,000)</td>
<td>-</td>
</tr>
<tr>
<td>IIR</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2.2 Malaria Genome Data sharing</td>
<td></td>
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</tr>
<tr>
<td>2.3 Data modelling fellowship</td>
<td></td>
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<tr>
<td>2.4 Piloting TDR grants (Control Academic collaboration)</td>
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<td></td>
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<tr>
<td>2.5 SDF Ebola</td>
<td></td>
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<tr>
<td>RCS</td>
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<tr>
<td>3.4 EDCTP Ebola Research</td>
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<td>3.5 RCS in (No Suggestions) countries in Africa</td>
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<tr>
<td>VES</td>
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</tr>
<tr>
<td>1.2 SDF Gender</td>
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<td></td>
</tr>
<tr>
<td>1.3 SDF Vector control</td>
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<tr>
<td>1.4 Caribbean Health Network</td>
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<tr>
<td>1.5 Environ public health</td>
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<tr>
<td>1.6 Platform for VBD courses</td>
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## 10. TDR funding in 2015

*Preliminary figures*

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*Contributors providing specific project funding*

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