Report of the third meeting of the WHO Diagnostic Technical Advisory Group for Neglected Tropical Diseases

Virtual meeting, 3 June 2021
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Contents

Abbreviations and acronyms iv
1. Introduction 1
  1.1 Declarations of interest 1
2. Background 1
  2.1 Meeting objectives 1
  2.2 Priorities for 2021 2
3. Global investment case 2
4. Updates from disease-specific subgroups 3
  4.1 Onchocerciasis 3
  4.2 Skin NTDs 3
  4.3 Soil-transmitted helminthiases 4
  4.4 Schistosomiasis 5
  4.5 Lymphatic filariasis 5
  4.6 Human African trypanosomiasis 5
5. Cross-cutting subgroups 6
  5.1 Clinical diagnosis, imaging and microscopy 6
  5.2 Manufacturing and regulatory pathways 6
  5.3 Surveillance 7
6. Resource mobilization subgroup 7
7. Human African trypanosomiasis biobank 8
8. DTAG open session conclusions 8
9. DTAG members closed session follow-up discussion 9
10. Third DTAG meeting follow-up meeting 10
  10.1 Attendees 10
  10.2 Discussion and recommendations 11
11. Recommendations 16
  11.1 Open session recommendations 16
  11.2 Closed session recommendations 16
  11.3 Follow-up discussion recommendations 16
Annex. List of participants 17
Abbreviations and acronyms

CDIM clinical diagnosis, imaging and microscopy
CL cutaneous leishmaniasis
DTAG Diagnostic Technical Advisory Group for Neglected Tropical Diseases
EDCTP European and Developing Countries Trials Partnership
EQA external quality assessment
FIND Foundation for Innovative New Diagnostics
HAT human African trypanosomiasis
IVDR In Vitro Diagnostics Regulation (European Union)
M&E monitoring and evaluation
MARP monitoring and regulatory pathways
NIH National Institutes of Health
NTD neglected tropical disease
PKDL post-kala-azar dermal leishmaniasis
QA quality assurance
QC quality control
RDT rapid diagnostic test
STAG Strategic and Technical Advisory Group for Neglected Tropical Diseases
TPP target product profile
VL visceral leishmaniasis
WHO World Health Organization
1. Introduction

Due to the ongoing coronavirus disease (COVID-19) pandemic, the third meeting of the Diagnostic Technical Advisory Group for Neglected Tropical Diseases (DTAG), an advisory group to the World Health Organization’s Department of Control of Neglected Tropical Diseases (WHO/NTD), was held virtually, on 3 June 2021.

The meeting was opened by Dr Mwelele Ntuli Malecela, Director, WHO/NTD, who offered thanks and congratulations to members of the DTAG and its subgroups on progress made since the DTAG began its work in October 2019. The DTAG plays an essential role in ensuring that diagnostics are available, field-ready and capable of supporting programme needs, while disease-specific subgroups have made significant progress in elaborating target product profiles (TPPs) for the development of crucial new diagnostics. The cross-cutting subgroups have now been launched and are poised to address critical issues in diagnostics that span the entire portfolio of NTDs.

The ongoing COVID-19 pandemic was seen to be a demonstration of what is possible in the diagnostics field when investment, innovation and collaboration combine. The DTAG is key to harnessing these resources to fill the diagnostic needs of NTD programmes.

The participants are listed in the Annex.

1.1 Declarations of interest

All the invited experts and observers were asked to declare any conflict of interest before the meeting. No conflicts of interest were declared.

2. Background

WHO/NTD manages a diverse portfolio of 20 diseases and disease groups, each with its own unique epidemiology and diagnostic challenges. Programmes to address each disease have different goals: disease control, elimination as a public health problem, elimination of transmission, or eradication. These programmatic goals may change over time as new tools are developed and global attention brings increased support.

In this context, the DTAG was set up to provide end-to-end support to WHO and the diagnostics community around the diagnostics agenda needed to facilitate progress towards achieving the targets set out in WHO/NTD’s high-level document, Ending the neglect to attain the Sustainable Development Goals: a road map for neglected tropical diseases 2021–2030 (“the road map”).

The DTAG’s brief includes more than just the tools themselves; it encompasses everything from biomarker discovery and assay development to laboratory and field validation leading to WHO endorsement, and issues relating to manufacturing, procurement, supply and deployment.

2.1 Meeting objectives

The objectives of the third DTAG meeting were described to the assembled participants. They heard that the subgroup chairs would provide updates on the progress of their groups and of the TPPs under development. The subgroup chairs were asked also to raise any issues or recommendations that amounted to key cross-cutting challenges requiring that they be addressed by the parent-level DTAG. Issues to be discussed at the third DTAG meeting included the need for biobanks to make samples available for test development and validation, and the need for standardized processes for laboratory and field validation.
The meeting was told that achieving real progress would require identification and engagement with new and existing donors to ensure that adequate resources were available to meet the needs of the various programmes. The DTAG would be asked to consider what steps the group might take to work alongside WHO on a shared advocacy strategy. The DTAG, it was stated, could play a vital role in supporting WHO as it made its case for investment in such tools.

2.2 Priorities for 2021

The following were identified as priorities for the DTAG in 2021:

- Draft a position paper or provide other technical support on how to deal with the challenge of imperfect gold standards in the context of test development.
- Standardize processes for test validation and WHO endorsement.
- Improve sample availability (biobanking).
- Coordinate with the Working Group on Monitoring, Evaluation and Research of WHO’s Strategic and Technical Advisory Group for Neglected Tropical Diseases (STAG) on the definition of new programmatic use cases.
- Work with WHO to make the investment case to advocate for new resources for diagnostics development.
- Support WHO to host a webinar to communicate diagnostic needs.

3. Global investment case

Dr Xiaoxian Huang presented an update on the global NTD investment case. This companion document to the road map estimates the funding required to address the critical gaps identified in the road map, and identifies and assesses the feasibility of mechanisms to raise additional funds and attract new partners.

The meeting heard that although funding requirements had previously been estimated, feedback suggested that it was difficult to make informed decisions based solely on lump sum figures. The investment case, therefore, would seek to focus on concrete investments needed to address the four critical priorities identified in the road map. The following questions were deemed key in terms of evaluating financial need:

- What are the priority actions that need to be supported with investments?
- How much is needed?
- How will success be measured?

Importantly, the investment case will not be disease-specific. Rather, its focus will be on system-level actions that create a solid foundation for diagnostics research and development across the NTD portfolio and the investment needed to support those actions.

The meeting heard that the DTAG subgroup chairs had recently participated in an early conversation about how best to proceed with the development of an investment proposal for diagnostics. A brainstorming process is under way to identify priority actions that may be proposed in the investment case. This work is at a very early stage and will require the close collaboration of the DTAG and its subgroups.
4. Updates from disease-specific subgroups

4.1 Onchocerciasis

Dr Marco Biamonte presented updates from the onchocerciasis subgroup. TPPs on elimination mapping and surveillance have been published. Other potential TPPs under consideration include those on:

- quality-assured polymerase chain reaction reagents for xenomonitoring (which could also be defined as a list of criteria, rather than a TPP);
- monitoring and evaluation (M&E); and
- transmission zones.

The subgroup's next steps involve drafting a manuscript on initial TPPs for submission to *PLOS Neglected Tropical Diseases*, and deciding whether or not to proceed with other potential TPPs.

The meeting was further told that the subgroup had found it somewhat difficult to find the published TPPs on the WHO website and that it would be helpful were WHO to post a table summarizing all of the TPPs in development, along with key features (such as sensitivity and specificity), status updates and links to the official publications as they become available.

The discussion following the presentation began with the process for developing new TPPs and whether or not DTAG endorsement was needed in order to proceed. From a WHO secretariat perspective, the meeting was told, TPPs should be based on identified gaps and needs within the programme. A strong rationale for developing new TPPs is required and the suggestion, therefore, was to raise potential TPPs for discussion with the onchocerciasis subgroup and the OTS. In the case of agreement that identified areas represented priority use cases for which TPPs were needed, the subgroup would be able to proceed with development.

Turning then to the question of each subgroup producing accompanying manuscripts, the meeting was told that these were not required but were recommended, given the sense that getting TPPs into the published literature is beneficial to the community because it provides scope for presentation of additional context to use cases and key discussion points.

Two subgroup action points were noted:

- **Action**: WHO/NTD knowledge management team to identify the best way to proceed with this suggestion.
- **Action**: Develop a TPP summary table for the WHO/NTD website to track status updates and links.

4.2 Skin NTDs

Isra Cruz presented the update from the subgroup on skin NTDs. The meeting heard that small, disease-specific working groups had been established to draft initial TPPs for each of the skin NTDs (Table 1).
Table 1. Status of TPPs for skin NTDs

<table>
<thead>
<tr>
<th>Disease</th>
<th>Use case</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buruli ulcer</td>
<td>Diagnosis at primary health care level</td>
<td>Sent to WHO to post for online public consultation</td>
</tr>
<tr>
<td>Dermal leishmaniasis (cutaneous leishmaniasis and post-kala-azar dermal leishmaniasis)</td>
<td>Point-of-care diagnostic test for dermal leishmaniasis</td>
<td>Sent to WHO to post for online public consultation</td>
</tr>
<tr>
<td>Leprosy</td>
<td>Diagnostic test to guide post-exposure prophylaxis in leprosy case contacts</td>
<td>Under DTAG review</td>
</tr>
<tr>
<td></td>
<td>Test to confirm the diagnosis of leprosy in patients with clinical signs and symptoms to guide multidrug therapy</td>
<td>Under DTAG review</td>
</tr>
<tr>
<td>Mycetoma</td>
<td>Diagnostic test to differentiate eumycetoma and actinomycetoma</td>
<td>Under DTAG review</td>
</tr>
<tr>
<td></td>
<td>Diagnostic test to determine when treatment can be stopped</td>
<td>Under DTAG review</td>
</tr>
<tr>
<td>Scabies</td>
<td>Starting mass drug administration</td>
<td>Sent to WHO to post for online public consultation</td>
</tr>
<tr>
<td></td>
<td>Stopping mass drug administration</td>
<td>Sent to WHO to post for online public consultation</td>
</tr>
<tr>
<td>Yaws</td>
<td>Detection of yaws cases</td>
<td>Incorporating DTAG feedback</td>
</tr>
<tr>
<td></td>
<td>Detection of azithromycin resistance</td>
<td>Incorporating DTAG feedback</td>
</tr>
</tbody>
</table>

This subgroup was also tasked with discussing the use of multiplex platforms for integrated management of skin NTDs. The meeting was told that with the input of biomarkers that are compatible with multiplexing and a common sample processing approach, it becomes possible to leverage multiplexing platforms for disease mapping, differential diagnosis panels, drug susceptibility testing, and disease surveillance. Subsequently, with the disease-specific requirements defined, the subgroup will be able to move forward in more concrete terms with regard to the requirements for a multiplex platform.

The discussion following the update considered imaging in the skin NTD group. The meeting was told that imaging will be addressed through the clinical diagnosis, imaging and microscopy (CDIM) cross-cutting subgroup, although it was likely that there would be close links between both groups.

On the question of whether post-kala-azar dermal leishmaniasis (PKDL) should be grouped with visceral leishmaniasis (VL) rather than cutaneous leishmaniasis (CL), the meeting was told that PKDL would be addressed in the VL subgroup. The dermal leishmaniasis TPPs preceded the DTAG, and, as a result, the group decided to take advantage of work already completed. It was noted too that there are a lot of biological similarities between PKDL and CL and important shared considerations such as detection of the parasite in skin. It would therefore make sense for PKDL to be considered alongside VL and CL.

4.3 Soil-transmitted helminthiases

Dr Bruno Levecke provided the subgroup’s update. He stated that the TPP for M&E was currently awaiting final publication by WHO and that consideration was being given to a subsequent TPP for *Strongyloides*.

Discussion concentrated on the absence of a gold standard, which poses significant challenges when assessing the performance characteristics of a test. The lack of access to well-characterized samples was also recognized as posing a challenge as further TPPs were taken forward into development. The meeting heard that a biobank is needed in order to ensure that manufacturers have access to the samples they need.
4.4 Schistosomiasis

The schistosomiasis subgroup update was provided by Dr Evan Secor. The meeting heard that TPPs for M&E and for surveillance were awaiting final publication by WHO and that the group was considering developing a subsequent TPP on female genital schistosomiasis.

4.5 Lymphatic filariasis

Dr Kim Won provided the DTAG with updates from the subgroup on lymphatic filariasis. The meeting heard that two initial TPPs developed by the subgroup (surveillance and stopping IDA [ivermectin, diethylcarbamazine citrate, albendazole]) had been published by WHO and an accompanying article submitted to *PLOS Neglected Tropical Diseases*. Further TPPs suggested included tools for lymphatic filariasis and *Loa loa* co-endemic settings as well as xenomonitoring tools. The meeting was told that discussions were ongoing regarding the need for new TPPs for these use cases.

The subgroup had been contacted by WHO to discuss a quality issue relating to the *Brugia* Rapid Test. In response, the subgroup developed a series of recommendations for the manufacturer, WHO, and the DTAG. These recommendations included a request to WHO to provide guidance on standardized laboratory and field validation and this was fed into the monitoring and regulatory pathways (MARP) cross-cutting subgroup agenda.

In discussion, the meeting heard that in addition to the need for defined validation protocols, it would also be helpful to understand requirements related to external quality assessment (EQA). EQA, the meeting was told, would also be a topic for the MARP subgroup.

4.6 Human African trypanosomiasis

The update from the human African trypanosomiasis (HAT) subgroup was delivered by Dr Enock Matovu and consisted of updates on TPPs (Table 2).

<table>
<thead>
<tr>
<th>Use case</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test for rhodesiense HAT in peripheral health Facilities</td>
<td>Submitted to WHO for final publication</td>
</tr>
<tr>
<td>Tool to identify individuals with suspected, but microscopically unconfirmed gambiense HAT</td>
<td>In development</td>
</tr>
<tr>
<td>Tool to assess <em>T. b. gambiense</em> infection in low prevalence settings</td>
<td>Planned</td>
</tr>
<tr>
<td>High throughput gambiense HAT test for verification of elimination</td>
<td>Planned</td>
</tr>
</tbody>
</table>
5. Cross-cutting subgroups

Following the updates from the various disease-specific subgroups, the meeting turned its attention to the DTAG cross-cutting subgroups, each of which reported in turn.

5.1 Clinical diagnosis, imaging and microscopy

The update was presented by Professor Michael Marks, who explained that the CDIM subgroup had been launched at the inaugural meeting in mid-May. Its 11 members possess a range of expertise including clinical medicine, microscopy and radiology. Initial conversations, the DTAG heard, had focused on understanding the range of topics encompassed by the subgroup’s remit, including platforms for image-sharing, methods for collecting and sharing images for diagnosis, and concerns regarding data security.

Priority activities identified included the following:

- definition of minimum image characteristics, quality standards, and metadata requirements for each of the imaging domains with the goal of developing a standardized framework for remote diagnosis;
- landscape analysis of tools, libraries and software that already exist across the different domains; and
- resources and training programmes.

In the discussion following the presentation the DTAG heard that the CDIM subgroup had an incredibly broad remit, and it was suggested that subdivision into smaller domains may make sense in the long run. However, preliminary steps with regard to landscaping and agenda-setting need to be carried out before that can be envisaged.

5.2 Manufacturing and regulatory pathways

The MARP subgroup update was presented by Dr Estelle Taute, who told the meeting that the subgroup’s first meeting had been held in mid-May and that it had included a series of high-level presentations on the WHO TPP development process, as well as presentations on prequalification for in vitro diagnostics and facilitated regulatory pathways. Discussion had been focused on the suitability of prequalification for NTD diagnostics, and concerns were shared regarding timelines and the ability to generate data similar in scope to other IVDs, given the comparatively small market for NTD products.

The meeting heard that the new European Union In Vitro Diagnostics Regulation (IVDR) was a potentially significant barrier to the availability of NTD diagnostics. This new regulation has much more stringent requirements than the CE mark process that it will replace, and this will lead to much higher costs for manufacturers seeking approval. The meeting heard that there had already been an example of a manufacturer dropping production of an NTD diagnostic as a result of this new regulation. The subgroup update ended with a statement that IVDR will be the subject of an in-depth presentation at its next meeting.
5.3 Surveillance

Dr Susan Montgomery presented the update. The surveillance subgroup was launched in mid-May and tasked with fulfilling the following objectives:

- to address the development of TPPs for assay platforms to test multiple analytes;
- to provide WHO with guidance on optimizing data use and survey design;
- to define new strategies to conduct surveillance in animal and vector populations, in order to monitor trends and species crossover events; and
- to improve the accessibility of new surveillance strategies.

Discussions at the first meeting had focused heavily on the need to balance disease-specific requirements with overall performance when testing for multiple analytes. The DTAG meeting heard that while the goal for a multiplex test should be to meet the minimum disease-specific requirements, experience had shown that this may not always be possible. This would constitute an important consideration during TPP development.

Survey design had also been raised as an essential component of integrated surveillance. Surveillance tools require a firm grounding within disease-specific M&E frameworks. Several methods for designing integrated surveys had been mentioned and these were marked as topics for further discussion at later subgroup meetings.

As an immediate action item, the subgroup decided to create a catalogue of surveillance needs by disease. This information would then be used to facilitate the development of TPPs, with the review to include considerations also on how to leverage surveillance platforms beyond the NTD sector (e.g. HIV).

6. Resource mobilization subgroup

Dr Hayato Urabe addressed the third DTAG meeting on behalf of the resource mobilization subgroup. It was established in December 2020 to bring together current and new donors active in the NTD diagnostics space in order to increase engagement and collaboration with the objective of strengthening the impact of investments in diagnostics through improved coordination, shared risk, and the leveraging of investments to maximize progress.

The first meeting culminated with a request for a landscape analysis of current and planned diagnostics investments funded by existing members of the resource mobilization subgroup. The DTAG meeting heard that the goal of the landscape analysis is to highlight gaps where innovation is needed in order to achieve the road map targets. The group’s data collection tool is currently undergoing pilot testing and is expected to roll out during late summer 2021.
7. Human African trypanosomiasis biobank

As for other NTDs, Dr José Ramon Franco Minguell told the meeting, the HAT community struggles with incentivizing manufacturers and researchers to develop diagnostics tools, given the lack of a large global market. Making samples readily available for both test development and later validation is one method for removing some of the barriers to test development. Also, as prevalence declines it becomes more difficult to access samples. Biobanking was therefore identified as a priority action for achieving HAT elimination.

The meeting heard that the Institut Pasteur (Paris, France) was selected to serve as the central repository for the HAT biobank. The main goal of this biobank is to provide reference clinical materials to research institutions to develop and evaluate new tests for the screening and diagnosis of HAT in low-resource settings. Development of the biobank was extremely complex, the meeting was told. It required everything from defining sample requirements and site selection to seeking ethical and regulatory approval from WHO as well as all of the institutions and countries involved. Training on sample collection, handling and transport was provided to approximately 85 individuals across the selected sites. To date, more than 22 000 samples (and accompanying metadata) have been collected and transported.

Sample transport constituted a significant challenge because it required cold chain management. Often, samples were collected in very remote areas and had to be transported to a central storage facility in-country before shipment to the Institut Pasteur. Once delivered to Paris, samples were validated and aliquoted into smaller quantities for storage.

The DTAG meeting was told that 45 sample requests have been received since samples became available in 2008. Requests are reviewed by an external committee and, to date, 34 have been approved. More than 9000 samples have been distributed to 28 research institutions.

Overall, establishment of the HAT biobank was reported to be a complex and costly process, although using an institution with expertise in biobanking was highly beneficial. There have been significant collateral benefits in terms of training, equipment and transportation capacity and, despite the challenges, the biobank has been unquestionably beneficial to the HAT community.

**Action:** Schedule follow-up session on biobanks.

8. DTAG open session conclusions

Following the biobank presentation, Dr Daniel Argaw Dagne proceeded to enumerate a number of DTAG meeting conclusions. It had been a highly productive meeting, he said, and progress since the last (second) meeting (13 October 2020) was encouraging. The meeting was told that WHO appreciates the recommendations and action items identified by the group and that the secretariat will work with the DTAG chair and members to organize an advocacy event. WHO will also work to develop a TPP status summary and repository for the WHO/NTD website. The meeting was further assured that the EQA issue raised during the course of the meeting would be sent for consideration and discussion to the MARP cross-cutting subgroup.
Professor Patrick Lammie began the closed session follow-up by underlining the necessity for more in-depth discussion despite a highly productive open session. He also stated that a separate discussion call would be set up within the coming weeks for items not addressed at the present meeting.

The closed session heard that most of the TPPs drafted had made allowances for laboratory-based tests and that this would have important implications in terms of requiring in-country laboratory capacity (both skilled personnel and equipment). The DTAG was therefore asked to consider whether it would be beneficial to establish a laboratory capacity subgroup or whether there might not be another mechanism by which this challenge could be addressed.

The meeting heard that WHO is aware of the lack of laboratory capacity in most regions and has now established a unit to help countries strengthen national laboratory capacity. There are various national or regional initiatives in this area (for example the African Society for Laboratory Medicine) but NTDs are rarely covered in their scopes of work. There are also existing laboratory networks, some of which include established quality assurance/quality control (QA/QC) systems. The meeting was advised that if DTAG moves ahead with a laboratory capacity subgroup, it will be important to discuss how best to collaborate with these groups.

Consideration ought to be given to two topics in particular:

- It would be helpful to consider how the DTAG can best support strengthening laboratory capacity. What sort of support can this group offer? Suggestions included: standardized protocols, training materials, QA/QC mechanisms, and support and integration with referral networks. The WHO secretariat would welcome feedback from the DTAG on how best to proceed.
- As conversations around laboratory capacity progress, it would be helpful to strive for a more complete understanding of what instruments or platforms are already in use so that what is in place can be built upon.

Further topics raised for subsequent follow-up discussion included:

- Laboratory capacity
- Advocacy

The meeting was advised that any advocacy plan or strategy must go beyond the traditional donor and scientific communities to include countries in which NTDs are endemic. The strategy must make considerations for advocating on behalf of directing resources towards NTDs within health ministries, despite competition with other health priorities. In many countries, a health ministry is more likely to act based on input from the medical community, rather than the scientific community. Advocacy and engagement strategies ought to be directed accordingly.

- TPP for dracunculiasis (Guinea-worm disease) eradication (testing of animals or infected copepods)
  This could be approached through a disease-specific subgroup or could be added to the agenda of the new zoonotic cross-cutting subgroup.
- Biobanking
  This is a broad topic that needs to be addressed at the overall DTAG level as well as at disease-specific level. Samples must be well-characterized in order to be useful, but guidance as to what “well-characterized” means will need to be generated.
• DTAG engagement with test developers
The meeting heard that subgroups would appreciate the opportunity to engage with test developers regarding some of these conversations. As discussed previously during the second DTAG meeting, specimens are scarce and it would therefore make sense to coordinate as much as possible to make the best use of limited resources. It would also be helpful to foster a spirit of collegiality rather than competition.

Action: A concept note on how this can be achieved will be circulated to the group.

10. Third DTAG meeting follow-up meeting

Following the initial open and closed DTAG sessions, a further follow-up meeting was held virtually on 15 June 2021.

10.1 Attendees
Present at this follow-up meeting were the following members of the DTAG and the WHO secretariat (see Annex for further details):

Marco Biamonte
Gautam Biswas
Rhea Coler
Isra Cruz
Daniel Argaw Dagne
Camilla Ducker
Xiaoxian Huang
Jonathan King
Annette Kuesel
Patrick Lammie Veerle Lejon
Mwelecele Ntuli Malecela
Fabricio Marchini
Michael Marks
Pascal Millet
Ashok Moloo
Rahma Noordin
René Paulussen
Anthony Solomon
Ashley Souza
10.2 Discussion and recommendations

Professor Patrick Lammie began the follow-up meeting by noting the productive nature of the previous two discussions and that time constraints had led to this follow-up session being scheduled to review the recommendations of the last meeting. Each recommendation was to be followed by a discussion period and recommendations updated according to feedback received before being sent to the WHO secretariat.

Recommendation 1

WHO should establish a DTAG subgroup to address critical issues related to the development and maintenance of laboratory capacity to support NTD programmes.

Discussion

Asked whether WHO had an inventory of existing WHO collaborating centres that support laboratory capacity and also whether there are existing EQA schemes, the meeting was told that this was not currently the case but that a review of collaborating centres is on the agenda for this year. Once the inventory has been completed, it would be helpful to understand if it makes sense to work with the collaborating centres to form a network among themselves, either formally or informally. Building on the collaborating centre would be a good start, the meeting was told, but using a network approach would allow for more widespread uptake of QA/QC practices.

With regard to laboratory capacity efforts ongoing in disease-specific communities, the meeting heard that the HAT laboratory community currently has a strong focus on EQA. Some of the systems that have been implemented include taking pictures and videos of rapid diagnostic tests (RDTs) and parasitological results, implementation of QC panels, etc. As for leishmaniasis, the laboratory community has taken similar steps such as implementing QC testing for RDTs and providing technical support to technicians. However, the actions undertaken really depend on the terms of reference for each collaborating centre. The Buruli ulcer laboratory network meanwhile has been formed with support from WHO and recently yaws experts have been invited to participate in the hope of future expansion.

The meeting heard that it would be extremely helpful to understand what networks currently exist as a starting point. A new DTAG subgroup on laboratory capacity could then look for opportunities to make high-level connections, rather than taking any sort of disease-specific approach.

A subgroup could help identify common challenges in capacity-building and make recommendations to address gaps, but building capacity requires a strong, well-budgeted institutional approach. Therefore, any potential subgroup should focus on broader networking, perhaps with the inclusion of work to strengthen the connection between peripheral and reference laboratories.

Institutional capacity must also roll up to national-level capacity so that countries are able to perform their own NTD testing. The focus should therefore be on forging networks between laboratories within countries to ensure high-quality data are available.

Other topics discussed following the first recommendation, and suggested for inclusion in a laboratory capacity subgroup, were as follows:

- A subgroup may represent a mechanism to leverage human resources to collect information on behalf of WHO.
- Development of WHO laboratory manuals, webinars, massive open online courses, etc.
- EQA (working closely with the MARP subgroup)
- Movement of samples between countries, transportation challenges that can result in sample degradation, regulations on the export of human samples.
Recommendation 2

Given that TPPs are developed based on the use cases established by NTD programmes and reviewed within the STAG Working Group on Monitoring, Evaluation and Research, the DTAG should establish regular (at least yearly) meetings with this working group (or similar mechanism) to review evolving M&E requirements for NTD programmes.

Discussion

The meeting heard that a considerable amount of effort has been put into the development of TPPs but that TPPs could become obsolete as programme goals and targets change. For example, the new HAT TPPs would look considerably different if an oral, single-dose medicine becomes available. It is essential that the DTAG is aware of these changes as they happen in order to make necessary adjustments on the diagnostics front. The meeting was told there should be regular reviews of the use cases with the M&E group so that potential changes can be flagged immediately.

Asked how the DTAG should go about establishing and formalizing this connection, the meeting heard that the WHO secretariat can facilitate the connection and should be kept informed, but it is important that the two groups work together directly, not through an intermediary. The chair of the DTAG attends the meetings of the Working Group on Monitoring, Evaluation and Research and a good first step would be to establish a reciprocal system.

Action: DTAG chair and WHO to work together with the chair of the STAG Working Group on Monitoring, Evaluation and Research to define the best mechanism for cross-collaboration.

Recommendation 3

WHO should develop and implement an advocacy plan to attract new resources to support the NTD diagnostics agenda.

Discussion

The meeting was told that in addition to the hard work and dedication of DTAG members, funding will be needed in order to truly make progress in diagnostics. The resource mobilization subgroup is an essential starting point, but this subgroup and the DTAG members also represent a potentially powerful resource. Members were therefore asked to look within their professional networks to identify potential sources of funding that may be able to be of service. In considering how best to engage with new donors, the DTAG was told that it needed to work closely with WHO to develop a clear advocacy agenda and standardized messaging.

Looking towards communication experts to help guide the development of advocacy materials and craft powerful messaging would be useful in this regard, just as a guided cohesive approach to advocacy would be more effective than a fragmented approach.

By the end of the summer, the meeting heard, it was likely that a majority of DTAG subgroups would have published at least one TPP. The next step then will be to draw in resources to take the TPPs forward into tool development. The DTAG must work closely with WHO to make this happen. It was suggested that a webinar be used to engage new donors and manufacturers and the meeting was told that WHO is willing to take this suggestion forward.

As for putting out communication materials and making needs known, the meeting heard that it is very difficult to access the published TPPs in the WHO Global Health Observatory. A suggestion was made during the first session to post a TPP status summary table on the WHO/NTD webpage, and this would certainly be beneficial and could be easily shared with partners.
WHO stated that it is trying to resolve the issues with its website by shifting to another system, in the hope of finding ways to make accessing the TPPs easier within the new system. In the meantime, a one-page dashboard that contains key details on the subgroups and TPPs would be a useful stop-gap. This might include the TPP status table with the diseases, use-cases, sensitivity and specificity requirements, status updates and links to final products. The dashboard could also include an organogram of the DTAG showing each of the different subgroups and list of key contact information.

**Action:** Develop a summary table and work with WHO to have it hosted on the WHO/NTD webpage.

The meeting then heard that for donor engagement and advocacy, the DTAG should look for other opportunities to share outputs; for example, as TPPs become available they should be shared with programme officers at the National Institutes of Health (NIH) and the European and Developing Countries Trials Partnership (EDCTP). The NIH could be an important resource, particularly for biomarker discovery.

**Action:** Share published TPPs with NIH (Pat Lammie).

The meeting then heard that as EDCTP is currently scoping out their next agenda, now would be a good time to reach out to them. Suggested contacts at EDCTP include Pauline Beattie, Michelle Helinski and Michael Makanga.

**Recommendation 4**

**WHO to work with the Foundation for Innovative New Diagnostics (FIND) and WHO collaborating centres to investigate the establishment of biobanks for priority NTDs.**

**Discussion**

The meeting was told that absence of samples that can be used for development and validation is a significant challenge. The samples that are available tend to be concentrated in research centres and redistribution can be challenging. Researchers and other partners should be encouraged to look towards the community benefit of collecting and archiving material as well as the metadata needed to make those materials useful.

With regard to biobanking, the meeting heard that biobanking should be expanded to include QC materials, that samples should be available in large enough volumes to support EQA programmes and that subgroups should note anticipated sample needs during the TPP development process. These inventories can then be used to guide decision-making and advocacy for biobanking.

It was further noted that work is also needed around standardization of consent procedures and specimen sharing. Groups such as FIND are already actively engaged in biobanking and have put a lot of effort into developing standard operating procedures and collecting material. The DTAG should seek opportunities to formalize connections to take advantage of resources that are already available.

It was also suggested that the DTAG should also consider removing “priority” from the wording of this specific recommendation.

The final point with regard to biobanking noted that there should be a strong regional component to the biobanking effort. Samples for foodborne trematodiases should be readily available in the South-East Asia Region. Chagas disease samples should be available in Latin and South America. The DTAG therefore should map out existing facilities to identify what is already available and where the gaps are.
**Recommendation 5**

DTAG to request the MARP subgroup to examine the implication of the new IVDR that will enter into application on 26 May 2022 on NTD diagnostics manufacturing and availability etc., and to propose ways to mitigate the negative impact.

**Discussion**

As previously discussed, the introduction of the new IVDR raises potentially significant barriers to the availability of NTD diagnostics. Even if WHO prequalification is expanded to include NTD diagnostics, this process is also extremely burdensome. The meeting heard that it would be extremely beneficial were the DTAG to advocate for a process similar to the COVID-19 emergency use authorization. A list of criteria is needed that are stringent enough to ensure high quality, but not so onerous as to become a significant barrier. With regard to the WHO Essential Diagnostics group’s involvement in these conversations, it was noted that the WHO secretariat will explore potential connections with this group.

The meeting heard that incentives to push test developers to work on NTDs were under discussion in the MARP subgroup, which has also identified a group member to prepare a presentation on the IVDR for the next (fourth) DTAG meeting. It was further noted that manufacturers should be engaged in these conversations. If they rely on funds provided by European agencies, that has implications as far as European regulatory approval is concerned, while national regulatory authorities may also insist on IVDR.

The meeting heard that there are examples of NTD diagnostics that have been used for years without regulatory approval and that the MARP subgroups should produce guidance on situations when it might be appropriate to seek regulatory approval as well as situations where this might be less relevant. The use case will be a significant factor in this regard.

**Recommendation 6**

DTAG to request that the chairs of the disease-specific subgroups address the challenge of test validation in the absence of a gold standard.

**Discussion**

As previously noted by the meeting, this is a huge challenge in moving from less sensitive to more sensitive tests; parasitological tests cannot be used as the gold standard for molecular tests.

Subgroups would benefit from dedicated statistical support in this regard because all of the statistical methods for dealing with this issue have their pros and cons. The meeting was told that experts should be engaged to provide information on the available methods and associated benefits and restrictions. The DTAG could then adopt a consensus view on the strengths and weaknesses of each.

Specifically, it was suggested that members identify experts to serve as technical resources and that this discussion include both a cross-cutting and a disease-specific approach. In some cases, a composite gold standard may be appropriate, but that may not be appropriate for each disease. The cross-cutting conversation may come first; that way the DTAG could review all of the available methods and produce some sort of guidance or endorsement. Then each disease-specific subgroup might discuss how the recommendations apply to their specific tools. The meeting then heard that the DTAG should have a stance on whether each approach is appropriate before working with the subgroup chairs to move forward.
Recommendation 7
DTAG to encourage disease-specific subgroups to convene meetings of test developers to promote information- and specimen-sharing.

Discussion
Discussion of recommendation 7 began by noting that test manufacturers currently work in relative isolation. There is little in the way of collaboration, but often they deal with similar issues. For example, many are trying to access the same samples or will need to do the same types of field evaluations. The disease-specific subgroups therefore present a mechanism to encourage information-sharing during the development process and to improve coordination with regard to issues such as access to samples.

Participation in a collaborative process would, however, be voluntary, of course.

It was suggested that a seminar or conference specifically for NTD diagnostic test manufacturers and researchers would be useful, on the proviso that all test developers be invited, not just the known ones.

It would make sense, the meeting heard, to engage manufacturers at disease-specific subgroup level; however, relationships would really need to be cultivated at the level of the parent DTAG. The disease-specific conversations, however, may not be appropriate for manufacturers working on multiplex tests.

The meeting was told that during its first meeting the surveillance subgroup had discussed at length the trade-off that is often required between meeting the requirements of individual diseases and having a useful multiplex test. Manufacturers, it was noted, may be aided in their understanding of those trade-offs without undue influence from any one group.

Recommendation 8
DTAG to recommend development of a TPP for dracunculiasis (Guinea-worm disease) under the newly formed zoonotic group.

Discussion
The DTAG follow-up meeting heard that the guinea-worm disease community has identified the need for a TPP for the detection of a serological response in dogs and non-human primates. This might be accomplished either through another disease-specific subgroup or through the new zoonotic cross-cutting subgroup.

The meeting discussed which instance would be best placed to carry out the work, hearing that if the appropriate expertise is (or can be made) available, then the zoonotic group may be asked to do it. Regardless of the entity actually carrying out the work, however, the meeting was reminded that the important thing was to ensure that TPPs are appropriately designed to deal with the sampling of veterinary populations. While this is a relatively narrowly-defined field, it does represent a chance to move into the One Health arena and, given the cross-cutting possibilities, the meeting heard the suggestion that the cross-cutting group would be the most appropriate entity to carry out the work.

On the specific subject of One Health, the meeting heard that One Health is included in the terms of reference of the subgroup on surveillance. The surveillance group was supposed to cover human, animal, vector and environmental surveillance, while the zoonotic group was initially intended to be a One Health group. It may be appropriate, therefore, to expand it now to be a One Health group since it has not yet formally started its work.

Action: WHO secretariat to make a recommendation on where One Health fits, either in the surveillance or zoonotic cross-cutting subgroups.
11. Recommendations

Following the initial open and closed DTAG sessions, a further follow-up meeting was held virtually on 15 June 2021.

11.1 Open session recommendations

Action: Schedule a follow-up session on biobanks.

Action: WHO secretariat to work with the DTAG chair and members to organize an advocacy event, either as a webinar or participation in a global advocacy event.

Action: WHO to develop a TPP status summary and repository for the WHO/NTD website.

Action: EQA issue raised during the course of the meeting to be sent for consideration and discussion to the MARP cross-cutting subgroup.

11.2 Closed session recommendations

Action: Engage with test developers to encourage collegiality rather than competition; concept note on how this can be achieved to be circulated to the DTAG group.

11.3 Follow-up discussion recommendations

Recommendation 1: WHO should establish a DTAG subgroup to address critical issues related to the development and maintenance of laboratory capacity to support NTD programmes.

Recommendation 2: Given that TPPs are developed based on the use cases established by NTD programmes and reviewed within the STAG Working Group on Monitoring, Evaluation and Research, DTAG should establish.

• Action: DTAG chair and WHO to work together with the chair of the Working Group to define the best mechanism for cross-collaboration.

Recommendation 3: WHO should develop and implement an advocacy plan to attract new resources to support the NTD diagnostics agenda.

• Action: Develop a summary table and work with WHO to have it hosted on the WHO/NTD webpage.

• Action: Share published TPPs with NIH (Pat Lammie).

Recommendation 4: WHO to work with FIND and WHO collaborating centres to investigate the establishment of biobanks for priority NTDs.

Recommendation 5: DTAG to request the MARP subgroup to examine the implication of the new IVDR that will enter into application on 26 May 2022 on NTD diagnostics manufacturing and availability etc., and to propose ways to mitigate the negative impact.

Recommendation 6: DTAG to request that the chairs of the disease-specific subgroups address the challenge of test validation in the absence of a gold standard.

Recommendation 7: DTAG to encourage the disease-specific subgroups to convene meetings of test developers to promote information- and specimen-sharing.

Recommendation 8: DTAG to recommend the development of a TPP for dracunculiasis (Guinea-worm disease) under the newly formed zoonotic group.

• Action: WHO secretariat to make a recommendation on where One Health fits, either in the surveillance or zoonotic cross-cutting subgroups.
Annex. List of participants

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