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

Virtual meeting, 8–9 November 2022
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### Abbreviations and acronyms

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<tr>
<td>DTAG</td>
<td>Diagnostic Technical Advisory Group for Neglected Tropical Diseases</td>
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<td>ERPD</td>
<td>Expert Review Panel for Diagnostics</td>
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<td>FIND</td>
<td>Foundation for Innovative New Diagnostics</td>
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<td>IVD</td>
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<td>NTD</td>
<td>neglected tropical disease</td>
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<td>PQP</td>
<td>Prequalification Programme</td>
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1. Introduction

The WHO Department of Control of Neglected Tropical Diseases (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 of these diseases have different targets according to the particular disease's profile: control, elimination as a public health problem, elimination of transmission, or eradication. Programmatic targets may change for any particular NTD over time as new tools are developed and global attention brings in increased support.

In spite of the diversity of disease programme targets, it was felt that there were common areas across programmes that would benefit from the establishment of a single working group for diagnostics. The Diagnostic Technical Advisory Group (DTAG) was formed to mould a unified approach for identifying and prioritizing diagnostic needs, and to inform WHO strategies and guidance on NTD diagnostics.

The first meeting of the DTAG was held at the Inter Parliamentary Union in Geneva, Switzerland, in October 2019. The second took place virtually in October 2020, the third in June 2021, and the fourth in October 2021.

Several disease-specific and cross-cutting DTAG subgroups have been formed, resulting in the development of target product profiles (TPPs) for new diagnostics, some of which have been published, and some of which are in production.

1.1 Meeting objectives

WHO/NTD convened the fifth DTAG meeting on 8 and 9 November 2022, with the following objectives across the end-to-end process of diagnostic development:

- to hear updates from disease-specific subgroups;
- to discuss progress made by the cross-cutting and resource mobilization subgroups;
- to discuss regulatory issues, including the pilot WHO Expert Review Panel for Diagnostics (ERPD) for NTDs;
- to discuss advocacy and resource mobilization; and
- to discuss engagement of manufacturers and developers.

The list of participants is annexed to this report.

1.2 Declarations of interest

Prior to the meeting, all DTAG members and invited experts completed declarations of interests forms for WHO experts, which were reviewed by the WHO secretariat. Only one expert declared an interest, which is under assessment for any potential conflict of interest. However, for the current meeting the declared interest did not warrant the exclusion of the expert from the meeting discussion.
2. Welcome and opening remarks

The participants were welcomed to the meeting and opening remarks were delivered by the DTAG chair.

2.1 General remarks

The meeting began with thanks to all DTAG members for their presence at the meeting and for their contributions to the DTAG’s activities since its inception in 2019. Progress has been made in all areas of the end-to-end process of diagnostic development, and potential new diagnostics are beginning to emerge as a result of this hard work.

There is also much work still to be done, the meeting heard, if the 2030 targets, laid out in *Ending the neglect to attain the Sustainable Development Goals: a road map for neglected tropical diseases 2021–2030* (“the road map”), are to be achieved. It was noted that the current meeting would hear reports about progress on these and other issues from key stakeholders and actors.

2.2 DTAG chair opening comments

The DTAG chair thanked the participants and members, noting that as this was the fifth DTAG meeting it was important to take stock of work to date – including overall progress thus far, progress with reference to specific diseases, and the progress of the cross-cutting subgroups. Advocacy and resource mobilization are also crucial, the meeting heard, and with prototypes being developed, it is important to identify manufacturers ready to work with the relatively low volumes and low margins associated with assays for NTDs.

The meeting was also reminded of the DTAG’s remit, which can be summarized as “encompassing the facilitation of new diagnostics end-to-end, from the initial scientific stages to eventual WHO approval and country uptake”.

3. Update on end-to-end support for NTD diagnostics

The meeting’s technical sessions began with an update on end-to-end support for NTD diagnostics. The DTAG was convened in order to assess and advise WHO on the diagnostic ecosystem. In practice, this means engaging with the process for diagnostics development from start to finish.

End-to-end diagnostics involve a number of discreet phases, from the definition of use cases to biomarker discovery through assay development, laboratory and field validation, assessment of likely demand, and stimulation of donor and manufacturer engagement, before a new diagnostic product ultimately receives WHO endorsement and can be procured by or for national programmes.

Typically, this process takes many years to complete; however, the imperatives imposed by the 2030 road map targets require the NTD community to work towards decreasing the time required to produce new diagnostics.

It was noted that, to date, one of the major achievements of the DTAG has been the development of a number of TPPs. These are intended as robust descriptions of the nature of future tests, to help guide development and validation.

Remarkable progress has been made across the NTD portfolio in developing and publishing new TPPs, and many more are in the works. These have now been collected on an NTD TPP dashboard (see section 5).
The meeting was told that as a result of activity around and relating to the DTAG, new investment in NTD diagnostics is being seen (from the Bill & Melinda Gates Foundation, for example) along with other new investments. This has led to a number of new prototype diagnostic assays entering the pipeline; the hope is that at least some of these will be translated into field use.

Throughout these steps, the meeting was told, it is important that standardized protocols and methodologies be developed and respected, to ensure that tests used to guide NTD programmes are of high quality and meet programme requirements. Such a systematic approach will provide clarity for test developers, as well as transparency and confidence in the process for the NTD community. It will ensure too that that new products meet TPP requirements, that performance claims can be independently verified, and that ultimately use cases and acceptability in the field can be assessed and confirmed. Many of these processes have already been piloted in work on lymphatic filariasis and visceral leishmaniasis (see sections 4 and 6).

The meeting then heard that clear pathways for programme use constitute a big challenge for the NTD diagnostic community. Given difficulties with approvals in jurisdictions of the European Union or the United States, for example, for products that are only intended for NTD endemic countries outside those zones, one important area of future work is the establishment of a WHO expert review panel which will constitute a new mechanism for the approval of diagnostic tests.

The status of the so-called missing pieces of the puzzle as it stands was then presented. Efforts are still ongoing, it was noted, to create a diagnostic landscape portal, in order to consolidate the information about the NTD diagnostic landscape.

Development of guidance on gold standards for the development of new tests remains a key issue, as does the need for a standardized dossier template for submissions to the ERPD (see section 7). There is also a continued need for advocacy to bring in new donors as well as engagement with manufacturers who can meet quality standards and cost targets.

These are all fields about which the fifth DTAG meeting expected to hear more information in the course of its deliberations; however, the meeting also noted that there is real optimism that the NTD community will be increasingly able to offer countries the tools and diagnostics they need.

4. Feedback from disease-specific and cross-cutting subgroups

During this session, the meeting heard updates from the chairs of the disease-specific and cross-cutting subgroups.

4.1 Disease-specific subgroups

4.1.1 Schistosomiasis

The Foundation for Innovative New Diagnostics (FIND) is in the process of attempting to define a composite reference standard for evaluating future schistosomiasis diagnostic tests. This work is being carried out in preparation for attempting to satisfy the TPP on monitoring and evaluation (1).

It is likely that a composite reference standard will be needed because current test formats (such as Kato-Katz and urine filtration) do not consistently achieve the required test sensitivity.
The schistosomiasis subgroup therefore proposes a composite reference standard comprising two days of microscopy for eggs, coupled with a day 1 PCR (polymerase chain reaction) test and a day 1 UCP-LF CAA (Schistosoma up-converting phosphor lateral flow circulating anodic antigen) assay. The composite reference standard has been agreed and proposed by the schistosomiasis subgroup, although the proposal will likely not be optimal for the other TPP for schistosomiasis (the TPP relating to elimination of transmission and surveillance).

The DTAG has plans to engage a consultant to work with the schistosomiasis and other subgroups to develop assay validation plans; following review and revision, these will be submitted to the Strategic and Technical Advisory Group for Neglected Tropical Diseases for review and endorsement.

For female genital schistosomiasis, a sub-subgroup has been set up and is in the process of defining use cases. It is likely there will be two use cases, based on the differential acceptability of visual inspection of the genital tract in different population groups.

Following the presentation, the meeting heard that the composite reference standard model is also likely to be of value for a number of other NTDs.

4.1.2 **Skin NTDs**

The TPP on Buruli ulcer (2) and the dermal leishmaniasis point-of-care TPP (3) are published. The leprosy TPPs for post-exposure prophylaxis and confirmation of diagnosis have been reviewed but are not yet available to the public.

Discussions are ongoing for a road map on leprosy diagnostics. Two mycetoma TPPs are publicly available (4), and the associated manuscript is to be published in a peer-reviewed journal. For scabies, the TPP for stopping mass drug administration is publicly available (5), and the manuscript has been published in a peer-reviewed journal (6). The yaws TPP has also been made publicly available (7).

The majority of the skin NTD TPPs, therefore, have now been published on WHO websites, and their scientific rationales published in peer-reviewed journals.

4.1.3 **Soil-transmitted helminthiases**

Planning has begun for the *Strongyloides* TPP, but drafting of the text has yet to start.

4.1.4 **Lymphatic filariasis**

Updates will be presented in the specific presentation on test evaluations (see section 6).

4.1.5 **Onchocerciasis**

Work is planned on the preparation of a TPP relating to quality-assured reagents for xenomonitoring.

4.1.6 **Dracunculiasis (Guinea-worm disease)**

Work is ongoing on two TPPs: one for a point of care test to detect infection in animal reservoirs of Guinea worm, and a second on detection in environmental samples.

4.1.7 **Visceral leishmaniasis**

Development of two TPPs is ongoing: one a point of care test for diagnostic confirmation and another for a test of cure after treatment. Draft zero versions were circulated to relevant parties at the beginning of November 2022 for review before publication. A smaller visceral leishmaniasis subgroup has been working on a standardized evaluation protocol of new laboratory tests.
4.1.8 **Trachoma**

After two meetings so far, the subgroup is part way through developing TPPs for three different use cases: one for programmatic use after discontinuation of antibiotic mass drug administration, one for evaluation units that are newly suspected of being trachoma endemic, and the third for evaluation units in which the epidemiology of trachoma is unusual. A third meeting of the subgroup will finalize these TPPs before they are posted on the WHO website for public comment.

4.1.9 **Human African trypanosomiasis**

The subgroup on human African trypanosomiasis has prepared its third and fourth TPPs, on an individual test to assess gambiense infection in low prevalence settings (8), and on a high-throughput test for gambiense infection and verification of elimination (9). Both have been through the period of public consultation and are now publicly available.

4.1.10 **Leprosy**

The leprosy subgroup has completed its TPPs; however, WHO internal ethical review is ongoing because the subgroup contains representation from the pharmaceutical industry. An in-depth conflict of interest enquiry is currently being carried out.

4.2 **Cross-cutting subgroups**

Since the fourth DTAG meeting (26–27 October 2021), and in response to a specific recommendation made during that meeting, the newly formed laboratory capacity subgroup was convened. Its first meeting will take place in the coming weeks.

4.2.1 **Clinical diagnosis, imaging and microscopy**

The subgroup has, on the clinical diagnosis side, been involved in establishing frameworks for validating clinical training packages for skin NTDs, given that this is a particular focus for national NTD programmes. Delphi processes are being carried out to establish minimum standards for these training packages. There will be interplay here with the concurrent work on gold standards for tests. If this is successful, and if work on incorporating artificial intelligence also proves useful, the hope is that significant progress can be made in tele-dermatology and in advanced clinical imaging to give particular support to the skin NTD field.

4.2.2 **Surveillance**

The subgroup has experienced both conceptual and logistical challenges since the last DTAG meeting. A planned landscape assessment, to explore what already exists in terms of integrated surveillance, and the subsequent development of a TPP, has been reassessed. The TPP was intended to address a technology-agnostic platform. Current thinking however is that it may be best to conduct the assessment without knowledge of what already exists. A lot of work is being done in this field and new developments are appearing regularly, such as the PAHO tool in the Region of the Americas. The meeting heard therefore that it makes more sense for the landscape assessment to take place after the TPP has been developed. The subgroup proposed developing the TPP and discussing this with the DTAG in due course. It will also look at a sampling framework for integrated surveillance before sending its TPPs for public consultation. The meeting heard that integrated surveillance is incorporated in many of the road map’s disease-specific targets for 2030 but remains a significant challenge. Concrete suggestions emanating from the surveillance subgroup would therefore be most welcome to the entire NTD community.
4.2.3 General

In concluding this part of the meeting, participants heard that the work of all the subgroups is continuing and that a huge array of expertise has been and is being continually mobilized; this amounts to some 150 experts that WHO is able to call on to move the work forward, amounting to a significant investment of people’s time to ensure that NTD programmes get the support they need. The meeting registered its profound thanks to all subgroup chairs and members.

5. FIND portal and WHO/NTD TPP dashboard

5.1 FIND NTD test directory tool

The meeting heard from FIND, the global alliance for diagnostics, which seeks to ensure equitable access to reliable diagnosis around the world.

FIND is currently working on an NTD test directory tool, developed jointly between its business intelligence and NTD teams.

FIND seeks to connect countries and communities, funders, decision-makers, health-care providers and developers to spur diagnostic innovation and to make testing an integral part of sustainable, resilient health systems. Echoing the principal DTAG theme, the meeting heard that diagnostic testing holds the key to elimination of NTDs. Indeed, the road map clearly highlights the diagnostic gaps that may prevent specific targets from being reached.

Collaborative efforts are needed, the meeting heard, as well as investment in existing diagnostics and a commitment to ensuring new levels of visibility for diagnostics. The context of country-driven initiatives will be important, too, in closing current diagnostic gaps.

The meeting then heard FIND’s articulated vision for the NTD test directory. This involves creating visibility around the diagnostic landscape for NTDs, and harmonizing multisectoral efforts by means of an open-access online portal for NTD diagnostics.

The portal will focus initially on seven NTDs – Buruli ulcer, Chagas disease, human African trypanosomiasis, lymphatic filariasis, onchocerciasis, schistosomiasis and visceral leishmaniasis – before eventually extending its scope to include all 20 NTDs.

Portal development will have two phases. Phase One will involve producing a fully searchable test directory and the meeting heard a request for developers and manufacturers to submit details of their tests, whether they are currently in development or commercially available. Phase Two will deploy data analytics to reveal insights from the data in the test directory. Users will be able to query the data on elements such as the number or type of diagnostics that are available for specific use cases or that relate to particular TPPs. It will also be possible to identify where there are diagnostic gaps.

The hope ultimately is that the portal drives advocacy, to address critical needs and funding gaps, but also to reduce the likelihood of duplication of efforts.

The meeting was told that three main components are required to build a fully searchable test directory. The first is a preparation process for data collection – building disease-specific data architecture and the online form construction. This is followed by data collection and data entry via landscapes and also via the online form – FIND, experts and companies feed in all the while, to draw attention to the tools that are currently available or in the development pipeline, including information about commercial availability and performance characteristics. After that, FIND and nominated experts will review the database of information received from the landscape analyses and online forms, before preparing the NTD portal with dashboards and finally publishing the portal on FIND’s web page.
The portal will operate in two main ways, the meeting heard. Data analytics will allow for selection and filtering of results or information can be downloaded for offline use.

Further maintenance and additions to the portal will require input from the global NTD community as new regulatory approvals or performance data become available. The meeting was told that the portal will only be as useful as the contributions that are made to it – and that this will require community involvement.

With limited financial and human resources, FIND welcomes all opportunities to work with WHO/NTD and disease experts to address these gaps.

Needs and requirements for the three components noted above were laid out for the benefit of meeting participants, as follows.

I. **Disease-specific database architecture**
   This will require time for disease leads/experts to review the Excel form and update it for their diseases.
   Estimated 2 days per disease (to be adjusted depending on the disease).

II. **Data entry/data collection**
   This will require input from consultants – estimated at US$ 15 000 per disease to conduct the landscape analysis.

III. **Data review**
    The Business Intelligence and Regulatory teams at FIND will contribute at a cost of some US$ 7500 per disease. This will require an estimate 15 days of work per year.
    The contributions of NTD disease leads are estimated to be needed at a rate of 5 days/year per disease.

5.2 **WHO/NTD TPP dashboard**

In response to a recognized need for accessible information, the meeting then heard that a list of currently available TPPs, along with links to the documents themselves and information about the status of TPPs in development, has now been published on a DTAG-specific webpage (10).

As new TPPs become available, these will be added to the dashboard, providing users and stakeholders with a one-stop resource for all diagnostic-related TPPs (11).

6. **DTAG second day session**

The meeting then turned to the question of standardizing test evaluations.

It is important, participants were told, that test developers understand expectations in terms of the amount of information required from them and also for end users to have confidence that new diagnostic tests have been evaluated appropriately. Impending development of new prototype tests will present case studies for standardized approaches to these evaluations; generic guidance is needed from WHO.

The meeting heard updates from the lymphatic filariasis group and then from the visceral leishmaniasis group about their work and aspects of that work which might provide the case studies referred to above.
6.1 Lymphatic filariasis test evaluation

The meeting heard information about the process the lymphatic filariasis group had been trying to follow, rather than specific details about the test itself.

In 2021, work began to determine if a prototype new lymphatic filariasis test was a suitable alternative to the test currently available to the global programme.

The principal challenge, it was noted, is the continuing absence of a gold standard diagnostic; this is an issue that affects much of the NTD portfolio. The group aimed to evaluate the equivalence of the new and old tests, not to compare against the established TPP parameters. However, some of the steps taken by the group may apply across the board. The process began with establishing the factors that would be needed for a laboratory evaluation and subsequently for a field evaluation.

For a laboratory evaluation, the group attempted to write a comprehensive generic protocol that might be adapted across the various sites. This included evaluation of key test performance characteristics, including diagnostic sensitivity and specificity, as well as the limits of detection and the sample type being analysed.

On the field side, again a generic protocol was drafted, and again a head-to-head comparison was instigated at the point of contact, with ease of use also being a key consideration for standardized assessment.

The meeting heard a number of issues and considerations relating to both the laboratory and field sides of the work. In the laboratory, these included the lack of a standard panel of samples, characterization of samples, direct comparison of the old and new tests, the potential for regional differences in pathogens and the number of labs and samples that needed to be included.

In the field, considerations included the identification of locations where there would be detectable signals, the nature of opportunistic or standalone activities – i.e., were there already planned surveys to which this could be added or would it necessary to start a new survey? Efforts were also made to develop a standardized supervision and training package. Ease of use in evaluation also required consideration of the order in which tests would be conducted in the field, as well as the number of sites and tests required to complete the dossier.

Given the lack of clarity around the process when it was begun, the team started slowly with one laboratory evaluation, and those data were subsequently presented to the lymphatic filariasis subgroup. Based on feedback, additional laboratories were selected based on identified gaps in the data. When those additional laboratory results became available these too were reviewed. In the field, efforts were made to encourage sites to summarize the results in a standardized way, with focus on test agreement and a standard ease of use form evaluating the feasibility of the test in the field. Consideration was then given at a meeting of investigators to the question of whether outcomes would have been the same or different using the two tests being compared.

To date, four laboratory evaluations have been completed, two country locations have been competed with another pending, and approximately 1250 head-to-head comparisons have been carried out.

The remaining steps of the process are now to summarize the laboratory results into a single report, to complete the planned field evaluation, to submit findings to the DTAG’s lymphatic filariasis subgroup for review and to seek guidance from WHO on whether there are enough data to support a decision to recommend the new test.

The meeting heard that the experience described in the presentation did indeed suggest the possibility for processes generalisable to other NTD groups. The meeting further heard that the laboratory and field protocols could conceivably be adapted for other, new diagnostic tests currently becoming available.
6.2 Visceral leishmaniasis test evaluation

The meeting heard that the process for visceral leishmaniasis test evaluation is similar to that presented for lymphatic filariasis.

Current evaluations related to a serological assay, and on the evaluation of rapid diagnostic tests for visceral leishmaniasis. Future visceral leishmaniasis diagnostics (nucleic acid amplification-based tests and assays with other types of target analytes) will be evaluated as per the terms of a TPP which is also currently under development.

The purpose of the current effort was, as in the case of lymphatic filariasis, to establish generic protocols for evaluation. Such a protocol, the meeting heard, would include provision for the evaluation of the intrinsic performance characteristics of the test and its applicability and equivalence per specimen type. Evaluations would also be carried out for accuracy, and to account for the limits of detection, and for the cross-reactivity and stability of reagents. The study site(s) and sample size remain to be selected.

The meeting was told that clinical performance studies will be carried out in the field, and that these will be evaluated for clinical sensitivity, specificity, positive and negative predictive values, and end-user feasibility.

For the serology test, a minimum number of sites will be proposed, representing all three disease foci (East Africa, the Indian subcontinent and South America). The meeting heard that WHO regional offices will coordinate, collaborating with local centres of excellence.

It was noted also that WHO is preparing standard operating procedures for field and laboratory evaluations of new diagnostic tests for visceral leishmaniasis.

Following the specific presentations, the meeting heard a suggestion that the generic protocols pertaining both to lymphatic filariasis and visceral leishmaniasis be taken as a modus operandi and that it might be possible to generate generic protocols for evaluations of tests which could be applied routinely, and adapted, to any and all NTDs. It was also noted in discussion that continued work was needed on the principle and practice of a gold standard for testing, given the likely preponderance of new tests arriving in the field.

The meeting then heard that the presentations on lymphatic filariasis and visceral leishmaniasis respectively underlined the importance of biobanks and that having sources of available material to enable generation of the panels needed for these evaluations is critical.

7. Expert review panel for diagnostics

The meeting then considered an issue of particular importance for the DTAG community, namely the pathway for bringing new tests into programmes. This has been under consideration by the DTAG since its inception.

The meeting was told that in-vitro diagnostics (IVDs) for NTDs pose issues for the community in terms of quality assurance for manufacturers and regulators and in terms of product selection dilemmas for procurers, donors and national programmes. WHO’s prequalification process for IVDs seeks to ensure products are quality-assured and appropriate for their intended use but hitherto it has been felt that NTDs were not sufficiently covered by existing guidelines.
In terms of risk classification, according to International Medical Device Regulations, many existing and potential new NTD diagnostic tests intended to facilitate decisions on individual-level treatment fall into risk categories C and D (C = High Individual Risk and/or Moderate Public Health Risk; D = High Individual Risk and High Public Health Risk), while many diagnostics used for population-based classification fall into categories A and B (A = Low Individual Risk and Low Public Health Risk; B = Moderate Individual Risk and Low Public Health Risk). The meeting heard that WHO prequalification of IVDs does not cover diagnostics that fall into classes A and B.

NTD diagnostics face a number of significant challenges. One such challenge is that their commercial development and production can be unattractive to manufacturers, given a burdensome regulatory pathway. The quality of many existing NTD diagnostics is sufficiently uncertain that a new EU regulatory framework for IVD medical devices has had an impact, despite its delayed implementation, to the extent that production of a number of test has been discontinued.

The meeting heard that NTD diagnostics are not currently within the scope of WHO PQ, and that indeed it was not realistic to include all NTD diagnostics within that scope. With regard to the end-to-end process referenced earlier in the meeting (see section 3), it is important that processes are as smooth as possible for diagnostics to be developed, the meeting heard, and this includes making it attractive for manufacturers to develop diagnostics for relatively small markets.

Currently, some NTD diagnostics in higher risk classes may enter WHO prequalification; however, backlogs are occurring due to the very large number of coronavirus disease (COVID-19)-related diagnostics being produced. Many diagnostics in lower risk classes have no independent quality assurance, the meeting was told. This creates financial, reputational and programmatic risks for procurers, donors and national disease control programmes. The meeting heard too that there is a risk for WHO, which purchases, distributes and recommends diagnostic tools to support national NTD programmes.

In the absence of a prequalification process, an ERPD serves an an interim mechanism for class C and D diagnostics and provides time-limited recommendations following review of the risks and benefits associated with procurement. The meeting was told that it had become apparent that there was a need to address this same issue for class A and B diagnostics.

It was proposed, therefore, that an NTD ERPD be set up in close collaboration with the WHO prequalification programme (WHO/PQP), and that priorities for such an expert review group would include looking at the lower risk-class diagnostics for lymphatic filariasis, onchocerciasis, schistosomiasis and yaws.

In practice, this would mean tailoring an ERPD to incorporate NTD expertise rather than creating an all-new panel. Although primarily intended for class A and class B NTD diagnostics, such a mechanism could also work as an interim measure for diagnostics in classes C and D, before these progressed to the prequalification process.

The mechanism proposed for the NTD ERPD would be run as a close collaboration between WHO/PQP and WHO/NTD. A proposed pilot phase for this is suggested and could be carried out for two new diagnostics coming on to the market, namely the rapid diagnostic tests for detecting the circulation of filarial antigen and the rapid diagnostic test to detect Leishmania. A small working group would be formed across NTDs and WHO/PQP to drive, analyse and report on the work being done.

The meeting then heard about the next steps in this regard, which included the plan for the ERPD pilot to start during the fourth quarter of 2022. WHO is currently working to modify and clarify guidance for the ERPD. There will also be a need to set out the pilot timeline and procedures to ensure that manufacturer performance evaluation data for the products of interest will be ready for review, also to ensure that independent evaluation data will be ready for review, to engage with manufacturers to ensure they are clear on what is required in the dossier, and to identify the experts needed for the ERPD. Each different diagnostic will require different experts to contribute to the ERPD.
The meeting was told that tests submitted for review will be assessed according to manufacturer-supplied data and independently obtained results. The ERPD is conceived as a risk-assessment process which will involve presentation of as much information as possible about the product, leading to an evaluation of whether the benefits of deployment outweigh the risks in any particular case.

With regard to the evaluation process being too restrictive for manufacturers, the meeting heard that the ERPD left some room for consideration of need, product and landscape. WHO prequalification is stringent – specifying sample sizes for specific locations etc – but the ERPD process would differ slightly, concentrating on the information that is already available as well as on manufacturers that have products that fit a given need. As such, the meeting was told, the ERPD will give the review process a certain degree of flexibility that will render it useful in a diverse diagnostic field.

The ERPD will concentrate in the main on practical solutions that give consideration to TPPs for specific products and diseases, so that manufacturers can take into account the TPP requirements as tests are developed. Manufacturers will receive questionnaires and information checklists, the meeting heard, although this will not be a formal, stringent regulatory authority dossier. The ERPD members, however, will assess a product’s level of adherence to the published TPP and decisions will be made accordingly, with a view to longer-term strict TPP adherence. The ERPD’s recommendations will have a term limitation too, and the meeting heard that the pilot and its results would be the subject of future DTAG meetings.

8. Advocacy and resource mobilization

Turning to advocacy and resource mobilization, the meeting heard that the disparate and wide-ranging nature of the NTD landscape makes coordination essential. Analysis and discussion of NTD diagnostics platforms by the subgroup identified a number of key issues, including the varying priorities that exist among the different funders, in terms of diseases, interventions and stages, the diversity of etiologies and intervention strategies for the respective diseases, the timing of fund availability and attendant constraints, and a possible lack of information-sharing which might lead to duplication of work and inefficiency of programmes.

Ideas discussed by the subgroup included setting up an advocacy and resource mobilization pooled fund as well as meetings to address diagnostic gap alignment and funding.

Again, the meeting heard, the idea of end-to-end support is key, from the early stages (research and development statistics through disease landscape and TPP lists and funder dashboards) to early-stage validation through clinical trials and the like, before eventual late-stage validation and regulatory approvals.

The subgroup is engaged in mapping the coordinated donor landscape as well as the coordinated manufacturer landscape. What links these together is the work on linking engagement with advocacy and only linking the various stages of the process can yield tangible results.

The meeting was then presented with a consolidated view of NTD-related activities planned for 2023, communicating with the DTAG the importance of sharing opportunities for advocacy, and the importance of working synergistically for strategic coordination of messages.

The next steps for the subgroup, the meeting was told, will involve seeking ways to continue to enrich the data available, to connect with other datasets, to establish a new platform or leverage an existing platform to this end, to coordinate advocacy efforts, to encourage co-funding and pooled funding mechanisms, and to identify opportunities for low cost and endemic-country manufacturing.
In discussion following the presentation, the meeting heard that advocacy is an ongoing and permanent task but that specific periodic engagement with manufacturers is also needed as part of an ongoing discussion. The meeting invited contributions on ways in which the DTAG can work with WHO to begin the advocacy process with manufacturers, noting that the explosion of rapid diagnostic tests for COVID-19 suggested that there is a huge amount of untapped potential which might be harnessed for NTDs.

The meeting heard that alongside the landscaping maps issued by various partners (see above), WHO also has clinical trial registries and the like which include some diagnostics information, as well as WHO databases on research and development.

The meeting noted a need for an active process in this regard to counteract an impression that much of this work has been passive in the past, noting too that a great deal of information is actually available but is not yet harnessed in such a way as to engage potential partners, manufacturers and other potential actors productively and proactively.

The meeting heard that better forecasts of the quantities of tests or units likely to be needed and/or consumed up to, for example, the year 2030 could give manufacturers a better sense of the scope of manufacturing needed, noting that the visibility and prestige associated with important steps in the elimination or eradication of certain diseases could prove attractive to manufacturers beyond the potential for economic profit.

The provision of information about realistic markets could also go a long way towards persuading manufacturers to engage with NTD diagnostics.

From a donor perspective, the meeting heard of the need for a joint NTD perspective, as opposed to individual NTDs advocating for individual diseases. The strength of the NTD community, it was suggested, is best represented when it acts in unison and when collective advocacy can be harnessed for specific impacts.

There was also a sense, the meeting heard, that manufacturers can be persuaded to engage. Some may be tempted by the idea of being leaders in this space, while others may be drawn to the challenge of acting in neglected areas; others may well require certain specific data before committing. It was noted that messaging may need to be more nuanced as a result of these considerations.

Manufacturers in NTD-endemic areas may be able to produce low-cost tests, but many tests have difficulties that need to be overcome – in terms of antigens, reagents, sample panels and other issues relating to quality control. Many manufacturers may feel excluded from the process, the meeting heard, for want of funding or guidance, not for want of good will.

DTAG members were urged to share information about manufacturers and contacts they may have at their disposal with the WHO secretariat.

9. Issues for discussion

Following the focussed presentations, a brief discussion session was opened, on topics not previously covered during the meeting.

Contributions centred around the importance for the DTAG and the NTD diagnostic community in general to consider the bigger picture and potentially make messaging clearer. One suggested focus was to recognize priority areas and needs that affected different parts of the diagnostic continuum – from our collective ability to define the problem faced to our ability to ensure proper care and treatment of a given disease.
The meeting also noted a need to talk about the detail of a lot of NTD work in conjunction with higher level trends and focuses such as equity and universal health coverage, and to seek out messages likely to resonate with the broader community.

The meeting noted that hearing experiences from the field tended to make instant converts of people with no prior knowledge of or expertise in NTDs and that finding ways to harness this could pay dividends.

10. Next steps and closing remarks

In concluding the fifth DTAG meeting, it was noted that these meetings give a sense to the NTD diagnostic community of what is coming together in terms of actions and initiatives and also of where additional attention is needed.

Referring to the end-to-end model for NTD diagnostics evoked at the beginning and during the presentations themselves, it was noted that significant progress has been made in developing TPPs but that there are also many use cases that have not yet been addressed, many of which fall under the zoonotic/One Health banner. The meeting noted this aspect as one requiring special focus in 2023.

It was further noted that there are particular opportunities in cases where the absence of a diagnostic is preventing the roll-out of an intervention, to ensure that resources are appropriately focused.

The meeting heard that as the community moves beyond TPPs and onto biomarker discovery and prototyping, much progress has been made – albeit on a narrow subset of NTDs to date – but there is still a lot of progress waiting to be achieved; in order to do so, there is a need for the NTD community to diversify.

It was noted that the FIND Portal, shared with the present meeting (see section 5) can be used to increase information-sharing and collaboration and that collaboration is crucial when it comes to validating new tests, for example.

The meeting noted a need to work across diseases more effectively, and for the establishment and use of well-resourced biobanks that manufacturers can use to quality-control their products. Progress has been made in validation and the meeting noted that 2023 would see generic standard operating procedure being generated to help the community know what is expected in terms of test validation.

The ERPD pilot is upcoming too (see above) and, if successful, and if processes can be standardized, will provide a clear pathway for diagnostic developers, and for the production of dossiers which will enable tests to get to the programmes where they are needed.

The meeting also noted a need for ambassadors in advocacy and resource mobilization, and for a need to explore novel pathways in attempting to secure resources.

A more collaborative environment is being fostered around diagnostics, the meeting heard, and this will accelerate approval and development processes.

The meeting was closed with grateful thanks to all presenters, participants and partners.

11. Closed session, 9 November 2022

During the closed session discussion on 9 November 2022, participants, made up of WHO Secretariat and the DTAG members, met to review the proceedings of the main DTAG session on 8 November 2022. In so doing, they discussed the presentations the main DTAG heard and their implications for the DTAG over the coming year, coalescing around a number of recommendations and resolutions.
12. Recommendations

The DTAG made the following recommendations, split here into category by relevant authority.

12.1 Recommendations for the DTAG and its subgroups

- Determine which use cases still require TPPs.
- Revisit the formation of the Zoonotic and One Health subgroup.
- Work with NTD focal points to estimate test demand forecasts by use case.
- Create two-page advocacy documents for each disease to describe the critical contribution that new diagnostics can make to achieving universal health coverage and the 2030 road map targets, starting with priority diseases.
- Accelerate the work of the laboratory capacity and networking subgroup.

12.2 Recommendations for WHO and DTAG

- Develop a slide deck to support advocacy for new diagnostics.
- Produce a landscape of platforms to advocate for NTD diagnostics development and access.
- Create engagement events for diagnostics manufacturers, funders, researchers, laboratory personnel and developers, including a calendar for potential engagement over the coming year.
- Accelerate and complete work on the following:
  - diagnostic gold/reference standards by NTD and by use case;
  - development of a dossier to support the ERPD;
  - lead and complete the ERPD pilot; and
  - develop biobank.
References


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