TARGET PRODUCT PROFILE

for a test for rhodesiense human African trypanosomiasis diagnosis usable in peripheral health facilities

World Health Organization

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Process of document development

The development of this target product profile (TPP) was led by the WHO Department of Control of Neglected Tropical Diseases (NTD) following standard WHO guidance for TPP development. In order to identify and prioritize diagnostic needs, a WHO NTD Diagnostics Technical Advisory Group (DTAG) was formed, and different subgroups were created to advise on specific NTDs, including a subgroup working on the human African trypanosomiasis (HAT) diagnostic innovation needs. This group of independent experts included leading scientists, public health officials and endemic-country end-user representatives. Standard WHO Declaration of Interest procedures were followed. A landscape analysis of the available products and of the development pipeline was conducted, and the salient areas with unmet needs were identified. Through meetings and remote consultations, the subgroup developed use-cases for the hypothetical tools considered as the main gaps, and gave them an order of priority. A template adapted to the HAT context was agreed and used for the development of the first draft of this TPP (priority N° 1) which underwent several rounds of review by the subgroup members. The ensuing version was reviewed by the DTAG members. Draft version 0.1 was posted on the WHO website for public consultation for 28 days with a proforma comment form. The final version received executive clearance on 7 June 2021.

Acknowledgements

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1. Background and medical need

Human African trypanosomiasis (HAT), also known as sleeping sickness, is a vector-borne parasitic disease caused by infection with protozoan parasites belonging to the genus Trypanosoma. They are transmitted to humans by bites of tsetse flies, found only in sub-Saharan Africa, which have acquired their infection from human beings or from animals harbouring human-pathogenic parasites.

HAT takes 2 forms, depending on the subspecies of the parasite involved:

- Gambiense human African trypanosomiasis (gHAT), caused by *Trypanosoma brucei gambiense*, found in west and central Africa, currently accounting for 95% of reported cases, has a chronic evolution. A person can be infected for months or even years without major signs or symptoms. When more evident symptoms emerge, the disease is often already in an advanced stage where the central nervous system is affected.
- Rhodesiense human African trypanosomiasis (rHAT), caused by *Trypanosoma brucei rhodesiense,* found in eastern and southern Africa, representing 5% of reported cases, is an acute illness with signs and symptoms observed generally a few weeks after infection. The disease develops rapidly, often provoking multi-organ failure and invading the central nervous system. Epidemic seasonal outbreaks are frequent.

HAT control is based on the screening of populations at risk for case finding and subsequent treatment in order to decrease the reservoir, complemented by targeted vector control in specific settings. Several tools are available or in the pipeline for the screening and diagnosis of gHAT, but similar tools for rHAT are either totally missing or losing ground in the evolving context.

Currently, there are no simple serological tests for rHAT screening and the diagnosis relies on the microscopic confirmation of trypanosomes in blood or other tissues, by either direct (blood, chancre or lymph node aspirate smear) or concentration methods in blood (capillary tube centrifugation or mini-anion exchange centrifugation technique) or cerebrospinal fluid (modified single centrifugation). These methods require a microscope and centrifuges, an electricity source and trained laboratory technicians.

The progressive introduction of rapid diagnostic tests for malaria has resulted in a decrease in the equipment and capacity for microscopy examinations in peripheral health facilities and consequently a reduction in the accidental diagnosis of rHAT, which was common when microscopy was done for malaria parasite detection.

A simple test for rHAT would facilitate the control and surveillance of the disease. In addition to faster prescription of a treatment, it may also help in capturing more information on the occurrence of rHAT transmission, hence recovering the loss of surveillance capacity and possibly strengthening it beyond the previous levels. For this, it would be important to be able to perform it at the location where people seek malaria diagnosis.

2. Use case

A test for diagnosis of rhodesiense human African trypanosomiasis (rHAT) usable in peripheral health facilities,[1] but other locations are conceivable.

[1] Peripheral health facilities: usually of low sophistication, located in the midst of, or at short distance from, communities at risk of rHAT.

3. Technical scope

Ideally, it should be an antigen detection test in a simple format (rapid diagnostic test), but it could also be a molecular test detecting DNA or RNA, or a microscopy-free test able to detect the presence of trypanosomes.

The test should provide immediate results for taking therapeutic decisions by confirming the presence of the infection, but, if not possible, it could be a screening test that, if positive, would be followed by confirmatory microscopic examination (taking into account that parasitaemia is usually high).

In the current context, confirmation is mandatory, but in a future with a safe, short regimen medicine allowing for widened treatment, a screening test to identify individuals to be treated would be desirable.