TARGET PRODUCT PROFILE

for a gambiense human African trypanosomiasis test to identify individuals to receive widened treatment

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 HAT TPPs. The draft of this TPP (rated as priority N° 2) 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.

Acknowledgements

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1. Background

Human African Trypanosomiasis (HAT) is a life-threatening parasitic infection transmitted by the tsetse fly, that is endemic in Sub-Saharan Africa. Having caused devastating epidemics during the 20th century, its incidence has fallen to historically low levels thanks to sustained and coordinated efforts over the past 20 years. Two trypanosome subspecies cause the disease, with distinct epidemiology: T*rypanosoma brucei rhodesiense* (*Tbr*), found in eastern and southern Africa, is harboured by wild and domestic animals which constitute its reservoir, being transmitted occasionally to humans; and *Trypanosoma brucei gambiense* (*Tbg*), in western and central Africa, with humans as the main reservoir, accounting for about 95% of the total caseload.

HAT diagnosis relies on laboratory techniques because clinical signs and symptoms are unspecific. Serodiagnostic tests exist only for *Tbg* and are based on the detection of specific antibodies, thus they are not confirmatory of infection. With the current low disease prevalence, the positive predictive value of serological tests is particularly low. Field-applicable tools include the card agglutination test for trypanosomiasis (CATT) used mainly in active screening by specialized mobile teams, and the rapid diagnostic tests that are more suitable for individual testing at point-of-care. Parasitological confirmation of *Tbg* infection requires microscopic examination of body fluids through laborious methods performed by skilled personnel. The best performing parasitological tests reach 85-95% diagnostic sensitivity at best but are more complex than tests with lower sensitivity.

In gambiense HAT (g-HAT) it has been observed since long that repeated rounds of serological screening followed by treatment of cases detected can bring down the prevalence to low levels, and this has been the cornerstone strategy of g-HAT control and elimination. But it is known that among seropositive but microscopically unconfirmed individuals there is a variable proportion that harbours the parasite and could perpetuate the reservoir. It has not been possible so far to recommend treatment on the basis of suspicion alone, because current treatments are logistically challenging and not sufficiently safe. The expected advent of a safer and easy-to-use treatment, would favourably tip the benefit-risk balance and allow for treating highly suspected individuals (widened treatment). A simple diagnostic tool to identify individuals eligible for treatment would be the ideal complement for a powerful elimination approach.

2. Use case

Diagnostic tool to identify individuals with suspected but microscopically unconfirmed g-HAT infection, eligible for treatment with safe and easy-to-use medicines.

3. Technical scope

It could be any method of high sensitivity but simple enough to be applicable at the point-of care. The sensitive parasitological methods currently used to confirm a *Tbg* infection are complex because they require specialized materials and equipment for concentrating the parasites, which often depend on a source of electricity, and which are often unavailable at the point-of care in HAT endemic regions. In the future, easier parasitological methods could arise.

The envisioned tool could be in any format, as long as it is simple and requires minimal specialized training.

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

4. Medical need

The safety profile and administration characteristics of the medicines currently available are not appropriate for their extended use in suspected but parasitologically unconfirmed cases. With the possible advent of a safe, effective and simpler anti-trypanosome treatment, it would be conceivable to widen the criteria of eligibility for treatment, to include individuals without parasitological confirmation but with a high degree of suspicion of harbouring parasites. Such type of "widened treatment" intervention would benefit infected individuals for whom the current diagnostic methods fail to confirm the infection. Simultaneously, it would benefit the community by further suppressing certain parasite reservoirs that perpetuate the risk of transmission.

The needed tool should identify individuals with a high degree of suspicion of infection (independently of symptoms) that can be considered sufficient to justify treatment with a medicine that has a good safety profile.

Ideally, with one test it should be possible to reach a therapeutic decision. A tandem of two simple sequential tests would also be acceptable.

Ideally, the test should be usable in peripheral health facilities[1], and in mobile labs at village level in zero infrastructure conditions.

A test fulfilling this profile, thought in relation to a safe and easy-to-use medicine that is expected to emerge with time, would nonetheless have a significant role even in the absence of such medicine.