Report of the third WHO stakeholders meeting on rhodesiense human African trypanosomiasis

Geneva, Switzerland, 10–11 April 2019
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<thead>
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<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAT</td>
<td>animal African trypanosomiasis</td>
</tr>
<tr>
<td>AU</td>
<td>African Union</td>
</tr>
<tr>
<td>CIRAD</td>
<td>Cooperation Internationale en Recherche Agronomique pour le Développement</td>
</tr>
<tr>
<td>CIRDES</td>
<td>Centre International de Recherche-Développement sur l’Elevage en Zone Subhumide</td>
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<td>CNS</td>
<td>central nervous system</td>
</tr>
<tr>
<td>CSF</td>
<td>cerebrospinal fluid</td>
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<tr>
<td>DNDi</td>
<td>Drugs for Neglected Diseases initiative</td>
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<td>DVS</td>
<td>Directorate of Veterinary Services</td>
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<td>ECCAS</td>
<td>Economic Community of Central African States</td>
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<td>FAO</td>
<td>Food and Agriculture Organization of the United Nations</td>
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<td>g-HAT</td>
<td>gambiense human African trypanosomiasis</td>
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<td>HAT</td>
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<td>HAT elimination Technical Advisory Group</td>
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<tr>
<td>IAEA</td>
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<td>ICIPE</td>
<td>International Centre of Insect Physiology and Ecology</td>
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<td>IEC</td>
<td>information, education and communication</td>
</tr>
<tr>
<td>MAAIF</td>
<td>Ministry of Agriculture, Animal Industry and Fisheries</td>
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<tr>
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<td>neglected tropical disease</td>
</tr>
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<td>OIE</td>
<td>World Organisation for Animal Health</td>
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<td>PAAT</td>
<td>Programme Against African Trypanosomiasis</td>
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<td>PATTEC</td>
<td>Pan African Tsetse and Trypanosomiasis Eradication Campaign</td>
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<tr>
<td>PCP</td>
<td>progressive control pathway</td>
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<tr>
<td>PCR</td>
<td>polymerase chain reaction</td>
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<td>r-HAT</td>
<td>rhodesiense human African trypanosomiasis</td>
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1. Introduction

2020 is the year set in the roadmap on neglected tropical diseases (NTDs), published by the World Health Organization (WHO) in 2012, as the target for elimination of human African trypanosomiasis (HAT) as a public health problem. In the London Declaration on NTDs, pharmaceutical companies, donors, endemic countries and nongovernmental organizations also committed themselves to meeting this goal. Joint work since 2000 resulted in 2018 in fewer than 1000 cases reported globally, a historically low number. Important milestones are being reached in achieving the goal of eliminating HAT as a public health problem by 2020.

Elimination efforts have focused on gamblense HAT (g-HAT), which is responsible for most (about 98%) reported cases. Rhodesienne HAT (r-HAT) is chronically neglected. The low number of reported cases fails to attract the interest of donors and r-HAT is thus of low priority for health decision-makers, despite its epidemic potential. Domestic and wild animal reservoirs make the control of r-HAT more complex. The One Health approach involving numerous sectors beyond human health, such as veterinary services, vector control, tourism and management services of protected areas, is the way forward to reach the set goals.

The first WHO stakeholders meeting on r-HAT elimination (Geneva, 20–22 October 2014) boosted the multisectoral coordination mechanism between WHO and partners to eliminate r-HAT as a public health problem. Contributing partners included members of academia, public–private partnerships, nongovernmental and international organizations, donors and national sleeping sickness control programmes. The second stakeholders meeting (Geneva, 26–28 April 2017) reviewed progress and identified essential activities for the future such as sustained surveillance, multisectoral coordination and partnerships, innovative methods and tools for control, and improving capacity-building.

This third stakeholders meeting took place as the first roadmap on NTDs (2015–2020) was almost concluded and the new roadmap on NTDs (2021–2030) was being prepared. It was the time to share the achievements, challenges and views on the goal of elimination among participating countries and implementing partners, and to advance the process of validation of elimination and strengthening of surveillance systems in order to detect any re-emergence of the disease before reaching epidemic levels again.

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2 The London declaration on neglected tropical diseases. Uniting to Combat NTDs; 2012 (http://unitingtocombatntds.org/resource/london-declaration).
2. Opening remarks

Dr Daniel Dagne, Coordinator of the Innovative and Intensified Disease Management unit, WHO Department of Control of Neglected Tropical Diseases, opened the meeting and called it a turning point, as the current roadmap on NTDs is almost concluded and the new Roadmap 2021–2030 is being prepared. He introduced Dr Mwelecele Ntuli Malecela, the new Director of the WHO Department of Control of Neglected Tropical Diseases, and Dr Augustin Kadima Ebeja, National Professional Officer of the WHO Country Office in Kinshasa, Democratic Republic of the Congo.

Dr Ebeja welcomed all participants on behalf of Dr Magaran Bagayoko, acting Director of the Communicable Diseases Cluster, and the entire NTD team in the WHO Regional Office for Africa. He reflected on the previous meeting and emphasized the One Health approach in r-HAT control. He highlighted that all stakeholders have an important role to play in their area of competence to face the challenges of the national control programmes. Finally, he thanked all the partners, whose commitment is greatly appreciated by the African regional office.

Dr Malecela emphasized the importance of the new NTD roadmap, the proposed goals and milestones for which are accessible online. Endemic countries, implementing partners, donors and stakeholders are invited to contribute and their input is crucial. The goals and milestones are due to be finalized in August 2019. She noted the significant progress of countries in which HAT is endemic towards elimination and the contribution of the Drugs for Neglected Diseases initiative (DNDI) to advancing drug development. However, elimination must be validated and surveillance strengthened. Government commitment and investment are essential to maintain that success, as is multisectoral involvement in a One Health approach. Dr Malecela closed her remarks by acknowledging the investment by all partners participating in this meeting.

The meeting was chaired by Dr Jorge Seixas, Portuguese Institute of Hygiene and Tropical Medicine, Lisbon. The meeting agenda is attached as Annex 1 and the list of participants as Annex 2.
3. Meeting objectives

The objectives of the meeting were:

- to sustain the commitment of national authorities and technical and financial partners to WHO’s objectives for r-HAT;
- to share achievements, challenges and views on the goal of elimination as a public health problem among countries and implementing partners;
- to discuss strategies for reinforcing control and surveillance of r-HAT;
- to assess the status of critical technical aspects in research, development and implementation of therapeutic and diagnostic tools, epidemiology and vector control; and
- to consolidate the network for collaboration and coordination among stakeholders.
4. The global situation of rhodesiense HAT

WHO has prioritized elimination of HAT under the Innovative and Intensified Disease Management unit. Two forms of the disease exist: g-HAT, the slowly progressing form, caused by *Trypanosoma brucei gambiense*, found in western and central Africa; and r-HAT, the faster progressing form, caused by *T. b. rhodesiense*, in eastern and southern Africa. HAT is transmitted through the bite of infected tsetse flies (*Glossina* genus). The goal of the HAT control and surveillance programme is to eliminate HAT as a public health problem by 2020. Since 2001, this elimination priority has been supported by a public–private partnership with Sanofi and Bayer.

Elimination of HAT (g-HAT and r-HAT) as a public health problem has been defined as fewer than 2000 cases reported per year at a continental level, and a 90% reduction of the total area at risk reporting more than one case per 10 000 people annually (from 2004 baseline levels). For g-HAT, the next goal is to interrupt transmission (i.e. achieve sustainable elimination of zero reported cases) by 2030. For r-HAT, the goal for 2030 is to maintain elimination as a public health problem (i.e. no area at risk reporting more than one case per 10 000 people annually). The pursuit of the goal for r-HAT is significantly more complex than that for g-HAT because of the predominance of animal reservoirs. The latest (2013) technical report of a WHO Expert Committee on control and surveillance of HAT\(^5\) states that complete elimination is not a technically feasible goal for r-HAT with the current means, but it does not rule out its elimination as a public health problem.

It is possible to eliminate r-HAT as a public health problem. Its occurrence is rare, and the current landscape suggests that some areas may be within range of this goal. The incidence of the disease is well mapped, particularly through the Atlas of HAT,\(^6\) which is an essential resource for monitoring progress but which may present an incomplete picture due to underreporting.

Elimination as a public health problem is a relevant goal as it helps to raise awareness of the disease and encourages countries to invest in its control. Several key elements of the WHO control programme revolve around: (i) providing support and technical guidance to countries endemic for the disease nationally to ensure access to diagnostic tools and treatment for all people at risk; (ii) strengthening surveillance by gathering and analysing all the data considered relevant to plan and monitor interventions; and (iii) coordinating stakeholders involved in r-HAT elimination. Importantly, reducing the number of cases is not an end-point in itself but rather the first step towards an integrated, sustainable surveillance programme. For this reason, the method of assessing this first step of elimination will be straightforward. Conversely, the process will be much more complex and stringent for assessing the interruption of transmission of the disease.

Since the reported 32 850 HAT cases in 2000, the number of cases has decreased significantly to < 2000 cases annually for the first time: 1446 cases were reported in 2017 (Figure 4.1). Most cases (77%) were diagnosed in the Democratic Republic of the Congo. In Guinea, the number of cases peaked at > 100 in 2016–2017, possibly due to the resumption of control activities after the Ebola crises. The data for 2018 are being finalized.

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but already show a decrease to < 1000 cases globally. National control programmes are thus well placed to reach the elimination goals by 2020. While the proportional contribution of r-HAT (2% of cases) to the global number of HAT cases is low compared with that of g-HAT (98% of cases), it must not be overlooked.

**Figure 4.1.** Numbers of HAT (g-HAT and r-HAT) cases reported annually since 2000, with the benchmark (2020) for elimination (expected cases)

![Graph showing numbers of HAT cases reported annually since 2000](image)

r-HAT is endemic in Uganda, the United Republic of Tanzania, Malawi, Mozambique, Kenya, Rwanda, Zambia and Zimbabwe. Since 2000, there has been a clear declining trend in the number of reported r-HAT cases: 31 in 2017 (from five endemic countries) and 24 in 2018 (from three endemic countries) (*Figure 4.2, Table 4.1*).

**Figure 4.2.** Numbers of r-HAT cases reported annually since 2001 at global level

![Bar chart showing numbers of r-HAT cases reported annually since 2001](image)
Table 4.1. Numbers of r-HAT cases reported by endemic countries, 2000–2018

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<td>Mozambique</td>
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<td>Namibia</td>
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</tbody>
</table>

From 2001 to 2017, Uganda reported more than half (58%) of the 5134 r-HAT cases globally. From 2013 to 2017, two countries (Uganda and Malawi) reported the majority of cases (46% and 39%) and three countries (the United Republic of Tanzania, Zambia and Zimbabwe) the remainder (Table 4.1, Figure 4.3).

Figure 4.3. Distribution of r-HAT cases in endemic countries, 2013–2017 (including exported cases)
The overall population at risk (i.e. the total number of people living in areas reporting > 1 case per 10 000 people annually) is constantly decreasing, but there remain 4.2 million people for whom the disease remains a public health problem. Currently, there are no populations at high or very high risk of r-HAT, but some remain at moderate risk (Figure 4.4).

**Figure 4.4.** Population at risk of r-HAT since 2000 and progression by five-year periods

While the coverage of the population at risk of infection has improved, a significant proportion still has difficulty accessing diagnosis and treatment for r-HAT. In 2017, some 124 fixed health facilities provided any diagnosis of r-HAT and 44 fixed health facilities provided treatment for r-HAT (Table 4.2).

**Table 4.2.** Health facilities providing r-HAT diagnosis and treatment in 2017, by endemic country

<table>
<thead>
<tr>
<th>Country</th>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Total</th>
<th>DxC</th>
<th>DxP</th>
<th>DxPh</th>
<th>Δ</th>
<th>Tx1S</th>
<th>Tx2M</th>
<th>Total</th>
<th>Δ</th>
<th>TOTAL</th>
<th>Δ</th>
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<td>12</td>
<td>124</td>
<td>13</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DxC, clinical diagnosis; DxP, parasitological diagnosis; DxPh, disease staging; Tx1S, first-stage treatment with suramin; Tx2M, second-stage treatment with melarsoprol; Δ, difference from previous year

Of the population at moderate risk of r-HAT in 2017, 87% lived less than 3 hours (94% less than 5 hours) away from a health facility capable of diagnosing r-HAT and 78% lived within 3 hours (89% within 5 hours) of a facility that provides treatment. Of the population at low risk, 69% lived less than 3 hours (84% less than 5 hours) away from a health facility capable of diagnosing r-HAT, and 62% within 3 hours (76% within 5 hours) of a facility that provides treatment.
One important caveat about the data on r-HAT is underreporting. The disease progresses rapidly, which makes it more difficult to detect cases because death can occur before patients reach a health care facility competent in diagnosis of HAT, especially if they live in a sparsely populated area.

Exported cases (i.e. cases diagnosed outside the country of infection) are infected mostly in touristic areas (e.g. national parks, wildlife reserves). Indeed, very few cases are reported from the local population in these same areas. All exported cases are reported to WHO, because only WHO enables access to treatment. WHO can use the reported number of exported cases as an indicator of the presence of r-HAT transmission in geographical areas.

There are no appropriate serological screening tools for r-HAT, and therefore detection of cases relies on clinical suspicion and parasitological diagnosis. It would likely be difficult to find a sponsor to develop a new serological screening tool. The low awareness of r-HAT and the lack of preparedness of health systems could also lead to misdiagnosis of the disease. Even in epidemic situations such as in Uganda during 1988–1990, mathematical models estimated that 39% of cases went undetected, and 92% of deaths were unreported. Furthermore, the increased use of rapid diagnostic tests (RDTs) for malaria, replacing examination by microscopy, has reduced the numbers of incidental r-HAT diagnoses through microscopy. It was pointed out that rotation of experienced laboratory staff also reduces capacities for diagnosis.

Health care workers should be sensitized to refer patients for microscopic examination in case of a negative RDT for malaria, as well as patients with positive RDT who are unresponsive to antimalarial treatment.

It was noted that great progress has been made towards the elimination goal and in reaching the defined milestones, even with deficient tools. Nonetheless, underdiagnoses and areas that are not well covered by control and surveillance activities, and thus where the situation is not well known, must be taken into account.

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5. Review of the conclusions of the previous meeting

**Box 5.1** summarizes the conclusions of the second stakeholders meeting (Geneva, 26–28 April 2017) and judges the progress of its recommendations. The start of a clinical trial to assess the efficacy of fexinidazole for treatment of r-HAT marks important progress, as does the development of tools to assess and validate the achievement of r-HAT elimination. Only some countries have forged collaboration and coordination of different sectors and reinforced national coordination bodies. Several recommendations have not been addressed, notably on improving surveillance, developing serological screening tools, tailoring target product profiles of vector control tools and increasing the use of blood smear microscopy.

**Box 5.1. Conclusions of the second WHO stakeholders meeting on r-HAT elimination in 2017 and whether the recommendation was followed ✓ or not followed ✗**

<table>
<thead>
<tr>
<th>CONCLUSIONS MEETING 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ It is necessary to improve surveillance by expanding country capacity for case detection.</td>
</tr>
<tr>
<td>✓ The development of better control tools is encouraged</td>
</tr>
<tr>
<td>✓ Development of serological screening tools is needed.</td>
</tr>
<tr>
<td>✓ Strong demand for extending the clinical trials of fexinidazole as a treatment for r-HAT.</td>
</tr>
<tr>
<td>✓ Target product profiles of vector control tools tailored to different environments are needed.</td>
</tr>
<tr>
<td>✓ The increased use of rapid diagnostic tests (RDTs) for malaria has reduced the use of blood smear microscopy, diminishing the possibility of diagnosing r-HAT. The use of blood smear microscopy in r-HAT endemic areas should be encouraged.</td>
</tr>
<tr>
<td>✓ WHO is requested to provide guidance on the requirements, procedures and criteria for assessing and validating the elimination of r-HAT as a public health problem.</td>
</tr>
<tr>
<td>✓ r-HAT endemic countries express their interest in gaining ownership of and promoting the use of the Atlas of HAT at national level, providing appropriate training material in English.</td>
</tr>
<tr>
<td>✓ Collaboration and coordination of different sectors including animal health, agriculture, conservation of natural areas, tourism and human health is required. The establishment and reinforcement of national coordination bodies is required</td>
</tr>
<tr>
<td>✗</td>
</tr>
</tbody>
</table>
6. Country status reports

6.1 Kenya

Current situation

Epidemics of r-HAT in Kenya have been interspersed with long periods of low endemicity across three main foci: the Lambwe Valley, western Kenya and the Masai Mara National Reserve. The cluster of cases detected in the early 2000s in western Kenya was drastically reduced in subsequent years in response to joint work by the governments of Kenya and Uganda in mobilizing local authorities and acting collaboratively. The two last cases reported were in 2012 from the Masai Mara National Reserve. Both cases (diagnosed in Belgium and Germany) were in stage 1 of the disease. After a massive response from multiple groups, no more cases have been detected in local people or tourists since then. No cases have occurred in the Lambwe Valley since 1992 and in western Kenya since 2009. Historically, reported cases from western Kenya have been in local people, whereas in Masai Mara the disease has been exclusively reported in tourists.

Endemic foci/regions at risk of r-HAT (Figure 6.1.1)

- Focus 1: Lambwe Valley (Ruma National Park occupies one-third of the valley floor);
- Focus 2: Western Kenya (Busia, Teso, Bungoma, Mount Elgon districts);
- Focus 3: Masai Mara area (Masai Mara National Reserve is 71 km from Serengeti National Park in the United Republic of Tanzania).
Figure 6.1.1. The risk of r-HAT in Kenya, 2012–2016

Health facilities capable of diagnosing r-HAT are concentrated in western Kenya, where historically most cases occurred (Figure 6.1.2). Clinical seminars to sensitize medical and laboratory personnel have been provided since 2012. In the Masai Mara National Reserve and its environs, personnel in six health centres were trained in 2012 (14 laboratory personnel and 71 other medical personnel). No cases have been treated in Kenya's public health-care system for at least 10 years, resulting in a lack of experience of medical and laboratory personnel in r-HAT. Furthermore, there is a shortage of diagnostic equipment, specifically centrifuges.
**HAT control activities: Ministry of Health**

- Activities are coordinated by the Vector Borne Disease Control Unit (VBDCU), formerly the Division of Vector Borne Diseases
- VBDCU has drafted an HAT elimination strategy
- Control and surveillance are being strengthened through capacity-building in existing health centres
- VBDCU coordinates governmental departments responsible for animal African trypanosomiasis (AAT) and vector control
- VBDCU is consulting with all relevant HAT stakeholders to prepare the dossier for validation of r-HAT elimination as public health problem by 2020
- Kenya has inaugurated an NTD Elimination Certification Committee
Health services have been devolved to County Governments (decentralization reform) since 2014, causing some loss of staff trained in HAT

National support and funding: other health needs are prioritized due to zero reported HAT cases

**Partners in HAT and funding from partners**

- The Government of Kenya provides human resources, financial and non-financial facilitation and coordination of HAT activities
- WHO provides antitrypanosomal medicines and supports surveillance of HAT
- The United States National Institutes of Health provides research funding
- The International Atomic Energy Agency (IAEA) provides research capacity-building and funding
- The United States Centers for Disease Control and Prevention funds HAT research and intervention
- DNDi provides capacity-building
- The Swiss Tropical and Public Health Institute provides capacity-building

**Other sectors active in tsetse and trypanosomiasis control**

- The Kenya Tsetse and Trypanosomiasis Research Council (KENTTEC) conducts tsetse control activities
- The Kenya Agricultural & Livestock Research Organization (KALRO) supports HAT diagnosis and surveillance, rapid response for suspected cases and oversees the development of new control tools
- The Kenya Wildlife Service focuses on Ruma National Park and the Masai Mara Game Reserve
- The International Centre of Insect Physiology and Ecology (ICIPE) conducts research on vector control tools
- The Directorate of Veterinary Services engages in veterinary services and disease control

**Challenges to r-HAT control**

- According to an assessment by VBDCU, 99% of health facilities and 98% of health workers in counties formerly endemic for r-HAT have no capacity to detect or diagnose HAT
- The absence of the disease contributes to low awareness among communities and health workers
- Expertise is being progressively lost through transfers and natural attrition, with no replacement of staff
- Diagnosis is complicated, and the current diagnostic tools are inadequate

**Future perspectives**

- Complete the r-HAT elimination strategy document led by VBDCU and the Ministry of Health of Kenya
- Strengthen diagnostic capacity for HAT in existing health facilities serving non-traditional foci (Masai Mara); provide training and programme support visits
- Continue to develop or adopt new tools for diagnosis and control
- Maintain vector control activities in relevant regions and enhance control of AAT (Kenya Tsetse and Trypanosomiasis Research Council, Directorate of Veterinary Services)
- Strengthen coordination of control efforts among partners through the One Health approach
- Provide equipment for data management and use these data to plan and monitor interventions (e.g. HAT Atlas)
- Create and maintain r-HAT awareness among community members
- Attend meetings of international focal points on HAT
- Synergize efforts to submit the dossier for validation of r-HAT elimination
6.2 Malawi

Current situation

Malawi has three foci of r-HAT transmission in the central, western and north-western regions (Figures 6.2.1–6.2.2). The numbers of reported cases fell to 11 in 2017 and 15 in 2018 (Table 6.2.1), most of which were from the Vwaza Game Reserve (Rumphi focus). Since 2016, cases have been reported in Nkhotakota Game Reserve again after 7 consecutive years without cases. It is assumed that r-HAT was reintroduced by imported cattle and elephants in 2014. The number of sites treating patients and the fatality rates are given in Table 6.2.2.

Figure 6.2.1. Distribution of r-HAT cases in Malawi, 2013–2017
Figure 6.2.2. The risk of r-HAT in Malawi, 2012–2016
Table 6.2.1. Reported cases of r-HAT, by focus in Malawi, 2014–2018

<table>
<thead>
<tr>
<th>Focus</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vwaza Game Reserve- 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases stage 1</td>
<td>3</td>
<td>20</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cases stage 2</td>
<td>30</td>
<td>5</td>
<td>31</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Total detected cases</td>
<td>33</td>
<td>25</td>
<td>33</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Kasungu National Park -2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases stage 1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cases stage 2</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total detected cases</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nkhotakota Game Reserve- 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases stage 1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Cases stage 2</td>
<td></td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Total detected cases</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Total for Malawi</td>
<td>36</td>
<td>25</td>
<td>35</td>
<td>11</td>
<td>15</td>
</tr>
</tbody>
</table>

Table 6.2.2. Numbers of treatment sites and cases treated, and fatality rates in Malawi, 2014–2018

<table>
<thead>
<tr>
<th>Treatment</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nr of sites treating patients</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Nr of cases treated</td>
<td>36</td>
<td>25</td>
<td>35</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Deaths</td>
<td>7</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Fatality rate (%)</td>
<td>19.4</td>
<td>12</td>
<td>5.7</td>
<td>9</td>
<td>13.3</td>
</tr>
</tbody>
</table>

Health facilities capable of diagnosing r-HAT

Vwaza Game Reserve
- Rumphi District Hospital; Katowo Rural Hospital and Mwazisi Health Centre
- Mzimba North District; Malidade and Thunduwike Health Centres

Kasungu National Park
- Kasungu District Hospital

Nkhotakota Game Reserve
- Nkhotakota District Hospital and St Anne’s Mission Hospital

HAT control activities developed by the Ministry of Health
- Screening services
- Diagnosis and treatment
- Community mobilization and awareness
- Promotion and facilitation of r-HAT research activities
- Resource mobilization
- Dissemination of programme performance
- Coordination with national and international partners
Control activities carried out by other sectors
- Ministry of Agriculture and veterinary services: treatment of sick animals
- Wildlife sector: responsible for tsetse control by setting traps in parks and game reserves
- Academic institutions: plan and conduct research, and disseminate results for policy change

Multisectoral organization and coordination
- National Trypanosomiasis Control Committee, secretariat is in the Ministry of Health
- Ministry of Agriculture, Irrigation and Water Development, Ministry of Public Works and Ministry of Natural Resources chair meetings alternatively
- Academic institutions write reports
- Good collaboration with departmental, inter-ministerial and other implementing partners and donors
- Local partners: ministries (Ministry of Agriculture, Irrigation and Water Development, Ministry of Public Works, Ministry of Natural Resources); academic institutions (Lilongwe University of Agriculture & Natural Resources College of Medicine, Kamuzu College of Nursing.
- Implementing partners: DNDi and WHO

Vector control activities
- Traps and targets cover only a few places in the three endemic areas
- In charge of the Department of National Parks and Wildlife

Challenges to r-HAT control
- Inadequately trained health workers
- Low-tech screening tools
- Cases reemerging in Nkhotakota Game Reserve after 7 years of no cases
- Lack of a utility vehicle at programme level
- The HAT programme is inadequately funded

Future perspectives
- Train HAT health workers in three districts
- Provide high-tech screening tools
- Increase community mobilization and awareness – brief traditional healers on HAT
- Ensure routine supportive supervision

6.3 United Republic of Tanzania

Current situation
The first recorded case of r-HAT in the United Republic of Tanzania was in 1922 in Maswa District, Shinyanga province. Large outbreaks in the north-western part of the country throughout 10 endemic regions have generated more than 90% of reported cases. The number of reported cases has decreased since 1995, with ≤ 5 cases reported annually since 2009 and even zero reported cases in 2018 (Table 6.3.1).
**Figure 6.3.1.** Distribution of r-HAT cases in the United Republic of Tanzania, 2012–2016

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**Foci/regions affected by r-HAT (Figures 6.3.1–6.3.2)**

- Tabora: Urambo, Kaliua
- Katavi: Mpanda
- Kigoma: Kibondo, Kasulu, Uvinza (Nguruka)
- Manyara: Magugu, Tarangire
- Mara: Mugumu, Serengeti

All have protected areas with nearby national parks.
Figure 6.3.2. The risk of r-HAT in the United Republic of Tanzania, 2012–2016

Table 6.3.1. Reported cases of r-HAT by focus in the United Republic of Tanzania, 2014–2018

<table>
<thead>
<tr>
<th></th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kigoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases stage 1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cases stage 2</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total detected cases</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tabora</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases stage 1</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cases stage 2</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total detected cases</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mara, Serengeti</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases stage 1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Cases stage 2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total detected cases</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total for Tanzania</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases stage 1</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cases stage 2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total detected cases</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>
Health facilities capable of diagnosing r-HAT (Figure 6.3.3)

- All district and regional hospitals
- All health centres
- A few dispensaries (private, refugee camps, faith based)

Figure 6.3.3. Location of health facilities with r-HAT diagnostic capacity in the United Republic of Tanzania, 2016

Table 6.3.2. Numbers of treatment sites and cases treated, and fatality rates in the United Republic of Tanzania, 2014–2018

<table>
<thead>
<tr>
<th>Treatment</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nr of sites treating patients</td>
<td>23</td>
<td>23</td>
<td>23</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Nr of cases treated</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>deaths</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fatality rate (%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
### HAT control activities: Ministry of Health

#### Coordination
- The epidemiology unit of the Ministry of Health, Community Development, Gender, Elderly and Children has a focal person for HAT
- The Ministry of Health, Community Development, Gender, Elderly and Children is a member of the One Health Coordination Unit in the Prime Minister’s office

#### Strategies
- HAT interventions are part of the NTD Master Plan
- National One Health Strategy, Guideline for Surveillance of Zoonotic Diseases
- National Strategy for Control of Tsetse and Trypanosomiasis (draft 2018)

#### Funding from partners
- WHO: for antitrypanosomal medicines, capacity-building and one desk top
- FAO: for development of a draft strategy for tsetse and trypanosomiasis control

### Multisectoral organization and coordination
- The One Health Coordination Desk, established in the Prime Minister’s Office, coordinates control of zoonoses, including HAT
- Six zoonotic diseases are prioritized, among them HAT
- A national strategy (guide) has been developed; each sector acts accordingly
- Partners in HAT coordination framework (One Health Coordination Desk): Ministry of Health, Community Development, Gender, Elderly and Children, Ministry of Livestock and Fisheries, Tanzania National Parks, National Institute for Medical Research, United States Agency for International Development, WHO, FAO and academia

### Vector control activities
- Generally small scale
- In national parks: tourism (Serengeti, Ngorongoro, Tarangire, Katavi)
- Methods used
  - impregnated targets (national parks)
  - spraying of tourist vehicles (national parks)
  - treatment of animals, e.g. using isometamidium bromide (in pastoral communities)
  - spraying of animals (in pastoral communities)
  - research on tsetse fly (vectors and vector-borne diseases)
- Responsible institutions: Tanzania National Parks, Ngorongoro Crater Conservation Area Authority, Ministry of Livestock Development and Fisheries, Department of vectors and vectors borne diseases in the Ministry of Health, Vector Control Training Centre Tanga

### Challenges to r-HAT control
- No coordinators at subnational level
- Very limited financial support to facilitate activities
Shortage of skilled staff (retired or inexperienced)
Overuse of RDTs decreases the utility of microscopy, some dispensaries do not have microscopes
Enormous associated social stigmatization
Long duration of hospitalization
Hard-to-reach areas

Future perspectives
Launch and operationalize the national tsetse and trypanosomiasis control strategy

- HAT surveillance and control activities planned
  - Rain laboratory technicians and clinicians in remaining HAT foci (including new suspected areas), invite District medical officers and sensitize use of microscopes
  - Advocate funding for tsetse and trypanosomiasis control to policy decision-makers
  - Conduct entomological and epidemiological surveys in new suspected areas (Mbeya, Singida)
  - Initiate a public awareness-raising campaign, including in schools in HAT-endemic areas

- Partnership for implementation
  - Strengthen collaboration among HAT stakeholders under the One Health umbrella
  - Identify and appoint tsetse and trypanosomiasis focal persons from key players in ministries
  - Establish a multisectoral Advisory Committee on tsetse and trypanosomiasis

In the discussion, it was acknowledged that many vector control programmes use pyrethroid insecticides.

6.4 Rwanda

Current situation
Although no cases of r-HAT have been reported in Rwanda since 1998, monitoring of the disease should continue. Historical data demonstrate that the disease was once present in the population,\(^8\) that the vector is still present in the country and that neighbouring countries still report r-HAT cases. Figure 6.4.1 shows the distribution of health facilities with capacity to diagnose r-HAT as of 2016.

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**Figure 6.4.1.** Location of health facilities with r-HAT diagnostic capacity surrounding the Akagera National Park of Rwanda, since 2016

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**HAT control activities: Ministry of Health**

- NTD Master Plan 2018–2024 (final draft), including r-HAT surveillance activities
- Key personnel on HAT and surveillance trained in 12 health facilities surrounding the Akagera National Park, in collaboration with WHO (August 2016):
  - surveillance tools (e.g. work plan, reporting registers) have been developed and shared with all sites
  - sensitization/awareness to the population in risk areas is being conducted
  - blood smear technique is used for laboratory diagnosis
  - HAT-positive slides are available for quality control at national and sentinel site levels
- Cascade supervision to monitor HAT surveillance system is integrated with other activities, by the NTD Programme, the National Reference Laboratory and WHO
- Funds are provided for essential materials; community sensitization and active case-finding

**Vector control activities**

- Animal health: Ministry of Agriculture and Animal Resources through the Rwanda Agriculture Board
  - 5000 traps for tsetse fly control have been installed in Akagera National Park
  - sensitization of farmers for bush clearing
  - Veterinary sector staff are on site to treat infected animals
  - laboratory is equipped for diagnosis of AAT, but no molecular testing has been conducted to date
○ Wildlife sector: The Rwanda Development Board, through the Akagera National Park, has procured traps for tsetse fly control
○ Partners in HAT and funding from partners: apart from governmental agencies, WHO is the main partner

**Challenges to r-HAT control**
○ Surveillance activities: quality control of health centres by hospitals and of hospitals by the National Reference Laboratory not yet systematically conducted. Semester Progress report meetings on HAT surveillance activities not regularly conducted within 12 sentinel sites and other 28 surrounding health centres
○ No formal framework for multisectoral coordination to conduct overall evaluation of implemented activities in surveillance of AAT and HAT
○ Financial: no recent research on HAT and on vector and species identification of AAT. Operational costs for progress and coordination meetings, mentorship, etc.
○ Human resources: additional key staff from other health centres surrounding the 12 HAT sentinel sites are not trained

**Future perspectives**
○ Conduct mentorship supervision and laboratory quality control
○ Enhance monthly reporting of activities
○ Create a multisectoral coordination framework for trypanosomiasis control (One Health approach)
○ Conduct a training of other key staff in health centres in at-risk zones
○ Advocate to create a communication channel with neighbouring countries
○ Advocate for resource mobilization for studies in trypanosomiasis and its vectors
○ Prepare a validation dossier for elimination of HAT as a public health problem

In the discussion, it was acknowledged that r-HAT appears to have been eliminated in Rwanda.

### 6.5 Uganda

**Current situation**
The numbers of reported cases have significantly decreased in recent years, with only 4 r-HAT cases reported in 2018 (Table 6.5.1). The most active focus was historically Lango, which reported 3 of the 4 cases in 2018 and where Kageramado is currently the area of concern. The recent emergence of new reported cases in protected areas, albeit in low numbers, is concerning. Evidence suggests that treatment of cattle with insecticides contributed to the rapid reduction of r-HAT cases in Uganda, although additional factors have not been fully explored.

**Endemic foci/regions with risk of r-HAT (Figures 6.5.1–6.5.2)**
There are 33 r-HAT endemic districts in Uganda in five major foci, in addition to protected areas, namely:
○ Ssese focus/region: Lake Victoria basin (Kalangala, Mukono, Buvuma, Buike, Kayunga)
○ Busoga focus/region (Linja, Iganga, Mayuge, Luuka, Kaliro, Buyenda, Kamuli, Namutumba)
○ Bukedi focus/region (Tororo, Butaleja, Busia, Namayingo, Paliisa, Kibuku, Budaka, Kibuku)
○ Teso focus/region (Bukedea, Ngora, Kumi, Serere, Soroti)
- Lango focus/region (Dokolo, Kaberamaido, Alebtong, Lira, Kole, Apac, Otuke)
- Protected areas (Queen Elizabeth National Park, Murchison Falls National Park) are isolated from other foci

Figure 6.5.1. Distribution of g-HAT (red) and r-HAT (blue) cases in Uganda, 2013–2017
Figure 6.5.2. The risk of g-HAT (red) and r-HAT (blue) in Uganda, 2012–2016
### Table 6.5.1. Reported cases of r-HAT by focus in Uganda, 2014–2018

<table>
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</table>
Health facilities capable of diagnosing r-HAT (Figure 6.5.3)
The location of HAT-competent health facilities follows the distribution of historical foci, creating a well-covered area:

- Namungalwe Health Centre III (Iganga district)
- Dokolo Health Centre IV (Dokolo district)
- Serere Health Centre IV (Serere district)
- Alebtong Health Centre IV (Alebtong district)
- Budopa Health Centre IV (Kamuli district)
- Lwala Hospital (Kaberamaido district)
- Nsiinze Health Centre IV (Namatumba district)
- Buikwe Health Centre IV (Buikwe district)
- Masafu Hospital (Busia district)
- Kitamiro HCIV (Buvuma district)
- Kibuku HCIV (Kibuku district)
- Mayuge HCIV (Mayuge district)

Figure 6.5.3. Location of health facilities with r-HAT diagnostic capacity in Uganda, 2016
Table 6.5.2. Numbers of treatment sites and cases treated, and fatality rates in Uganda, 2014–2018

<table>
<thead>
<tr>
<th>Treatment</th>
<th>2014</th>
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<th>2018</th>
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<td>10</td>
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<td>Fatality rate (%)</td>
<td>1.4%</td>
<td>7%</td>
<td>0%</td>
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</table>

HAT control activities: Ministry of Health

- Strategic framework: NTDs including HAT are covered by the national health policy, the health sector strategic and development plan and the NTD master plan
- Structural aspect: Department of Community Health and Division of Vector Borne Disease Control
- National Sleeping Sickness Control Programme: national programme manager; regional coordination office and district focal persons
- Coordination at country level: Uganda Trypanosomiasis Control Council (UTCC) with the Coordinating Office for Control of Trypanosomiasis in Uganda as its secretariat
- Partners: research institutions, academia and other governmental sectors (represented at UTCC), namely Makerere University, University of Gulu, DNDi, MAAIF (Ministry of Agriculture, Animal Industry and Fisheries), Uganda Wildlife Authority and international partners (University of Edinburgh)

Control activities carried out by other sectors

- Animal health: spraying of cattle, screening and treatment: Coordinating Office for Control of Trypanosomiasis in Uganda/Tackling Infections to Benefit Africa, academia (universities of Makerere, Edinburgh and Gulu), the private sector and MAAIF
- Wildlife sector: selective trap deployment
- Vector control: traps by MAAIF
- Others: sterile insect technique by MAAIF/IAEA/PATTEC

Challenges to r-HAT control

Operational challenges

- Ministerial: an inter-ministerial body (UTCC) exists but the contribution of the various ministries differs
- Financial: few resources are allocated due to competing priorities
- Human resources: staff transfers, other employment opportunities
- Multisectoral coordination: UTCC provides overall coordination for sectors involved but contribution is uneven
- Other: HAT surveillance in protected areas is a challenge

Future perspectives

HAT surveillance and control activities

- Maintain and reinforce ongoing passive surveillance
- Increase coverage of diagnostic services through peripheral health facilities where r-HAT is presently not routinely diagnosed
- Reorient health workers in r-HAT
- Sensitize communities to increase awareness about r-HAT
- Implement partnerships: DNDi, FIND, University of Edinburgh, Makerere University
6.6 Zambia

**Current situation**

Zambia has reported cases of r-HAT since the 1920s in three main foci, typically buffer zones close to game parks and protected areas (Figure 6.6.1). A total of 3 cases were reported in 2017 and 5 cases in 2018. The reemergence of the disease in various foci is of particular concern (Table 6.6.1).

**Figure 6.6.1.** Distribution of r-HAT cases in Zambia, 2013–2017

**Figure 6.6.2.** The risk of r-HAT in Zambia, 2012–2016
<table>
<thead>
<tr>
<th>Location</th>
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Table 6.6.1. Reported cases of r-HAT by focus in Zambia, 2014–2018
Table 6.6.2. Numbers of treatment sites and cases treated, and fatality rates in Zambia, 2014–2018

<table>
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**HAT control activities: Ministry of Health**

National Sleeping Sickness Control Programme:
- Under the Communicable diseases unit in the Ministry of Health, dealing with NTDs
- Focal point person in charge of NTDs
- National Coordinator appointed by the Permanent Secretary of the Ministry of Health

Partners in HAT control: WHO

**Multisectoral organization and coordination**
- Ministry of Health and University of Zambia, School of Veterinary Medicine, in evaluating the LAMP (loop-mediated isothermal amplification) test project
- One Health concept (Ministry of Health and School of Veterinary Medicine)

**Vector control activities**
- Aerial spraying of insecticides in Western region and insecticide-treated targets in national parks
- Responsible institutions: Ministry of Livestock and Zambia Wildlife Authority, Pan African Tsetse and Trypanosomiasis Eradication Campaign (PATTEC)/Government of Zambia.

**Challenges to r-HAT control**
- Frequent changes in focal point persons
- Drug distribution system
- Budgetary constraints, dependency on WHO
- Frequent transfer of trained laboratory technologists in endemic areas
- Weak multisectoral coordination
- Lack of quality control for r-HAT laboratory diagnosis, lack of regular refresher courses for laboratory technologists and lack of more sensitive laboratory diagnostic techniques such as Woo’s method (only available in one hospital)

**Future perspectives**
- Cross-border collaboration meeting with Malawi and Zimbabwe (Ministry of Health focal point persons and WHO country offices)
- Sensitization workshop for District Medical Officers from r-HAT endemic districts
- Development of IEC (information, education, communication) materials
- Refresher course for laboratory technologists, pharmacists and clinicians
- Establish quality control for laboratory diagnosis of r-HAT
6.7 Zimbabwe

Current situation

r-HAT is limited to one area in the Zambezi Valley (Figures 6.7.1–6.7.2). Since 2000, very few cases have been reported, but in 2012 some 9 cases were reported for unknown reasons. In 2017, 3 cases were reported whereas in 2018 there were no cases (Table 6.7.1). Historically, cases have been associated with proximity to the Zambezi River and wildlife, making the interface between wildlife and humans a major concern for risk of r-HAT. This is especially important as the area is used for safari hunting groups and hosts visitors to national parks. Tsetse flies are present in an area of 20 000 km² in the northern part of the country, and studies of their distribution show a pattern that closely matches the distribution of cases. Generally, diagnostic capacity remains poor in health-care facilities, especially in the affected area. Furthermore, there is no treatment facility for r-HAT in the focus area; cases are treated in Zambia or in hospitals in the capital city. Medicines are only dispensed in one pharmacy in Harare (which is > 200 km away from endemic areas). A well-established tsetse control division is involved in vector control through various methods.

Figure 6.7.1. Distribution of r-HAT cases reported in Zimbabwe, 2013–2017
Figure 6.7.2. The risk of r-HAT in Zimbabwe, 2012–2016

Table 6.7.1. Reported cases of r-HAT by focus in Zimbabwe, 2014–2018

<table>
<thead>
<tr>
<th>Focus</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Makuti focus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases stage 1</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Cases stage 2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total detected cases</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

HAT control activities: Ministry of Health

National Sleeping Sickness Control Programme:
- Under the communicable diseases unit in the Ministry of Health, dealing with NTDs
- Focal point person in charge of NTDs
- National Coordinator appointed by the Permanent Secretary of the Ministry of Health

Partners in HAT control: WHO

Multisectoral organization and coordination
- The Directorate of Epidemiology and Disease Control houses the NTDs unit
- Close, sustained collaboration with veterinary services in the Ministry of Agriculture (One Health, integrated vector control)
- Private physician and pharmacist conducting case management in Harare with support from WHO for supply (medicines are distributed free of charge)
- The National Health Strategy 2016–2020 and the National NTD Strategy 2012–2016 address NTDs
Control activities carried out by other sectors

- Animal health: dipping of livestock using deltamethrin, surveillance and control of AAT in accordance with the Progressive Control Pathway
- Vector control interventions

Vector control activities

Methods used:

- Tsetse surveys using Man-screen fly-rounds and traps
- Odour-baited insecticide-treated targets and insecticide-treated cattle
- Ground spraying (2012–2013)
- Sterile insect technique: entomological baseline data collection, drone release feasibility trial

Areas/regions covered

- Mola area adjacent to Matusadona National Park, north-west Zimbabwe; sterile insect technique project to be implemented in 1200 km² of the national park.
- Makuti HAT focus area (northern district)

Responsible institutions: Division of Tsetse Control Services – Department of Veterinary Services (Ministry of Lands Agriculture, Water, Climate and Rural Resettlement)

Challenges to r-HAT control

- Low level of awareness among management, professionals and communities about HAT
- HAT prevention, control, management is currently not prioritized
- No dedicated resources are available for HAT
- No training programme and hence no capacity to detect, confirm and treat HAT cases
- The supply of antitrypanosomal medicines by WHO is appreciated, but access is limited through centralization
- Poor surveillance for early detection and reporting of cases
- No case management guidelines

Future perspectives

- Establish a National Sleeping Sickness Control Programme within the NTD Taskforce
- Map the distribution of all partners with capacity to control, detect and manage r-HAT in the country
- Strengthen the rapid disease notification system for HAT surveillance, management and control activities
- Develop a joint reporting platform with veterinary services
- Re-map the geographical area of risk based on vector, parasite and human cases to better target control towards elimination.
7. Elimination of rhodesiense HAT as public health problem in 2020

7.1 Human African Trypanosomiasis Elimination Technical Advisory Group

The HAT elimination Technical Advisory Group (HAT-e-TAG) was established in 2016 to assist WHO in defining the criteria and procedures for the validation and verification of HAT elimination. The target for 2020 (i.e. elimination as a public health problem) must be validated. The target for 2030 (i.e. zero transmission of g-HAT) must be verified. For that, the status of HAT elimination in countries must be assessed against objective criteria and the achievement formally recorded. HAT-e-TAG reviews the indicators to assess the achievement of HAT elimination, devises templates for national dossiers on validation/verification and establishes the procedures to review the national dossiers. It also defines the procedures for post-elimination surveillance and revises the national status. The process is periodically reviewed, according to scientific advances and tools.

HAT-e-TAG comprises seven members, without conflict of interests, who are appointed for 2 years on the basis of their personal (not institutional) expertise, and six advisors who represent their organizations. The advisors do not participate in final decisions. Meetings are held annually at the invitation of WHO.

The first HAT-e-TAG meeting (Geneva, 23–25 November 2016) refined the target/indicators for elimination of HAT as a public health problem. The global target was originally defined as: < 1 new reported case/10 000 inhabitants per year in at least 90% of foci, with < 2000 reported cases per year at continental level. As foci are not objectively measurable, and as the area at risk of HAT can be better measured in a standardized way, HAT-e-TAG refined the target for 2020 as: a 90% reduction of the area at risk reporting ≥ 1 case/10 000 people per year. The primary indicators are thus the number of cases (as before) and the area at risk reporting ≥ 1 case/10 000 people per year. This new indicator was endorsed by the WHO Strategic and Technical Advisory Group for Neglected Tropical Diseases at its tenth meeting (Geneva, 29–30 March 2017) and is now the official metric. The 90% reduction refers to a baseline of the area at risk calculated over the 2000–2004 time-period. The secondary indicators (as before) are geographical distribution of HAT, level of risk of population, and coverage of surveillance and control.

The new definition of the indicator and target is appropriate at the global level. However, HAT-e-TAG advised that this particular indicator should not be established at a national level because it requires advanced expertise in geographical information systems and software, which national programmes often lack. As an outcome of the second HAT-e-TAG meeting (Geneva, 26–28 April 2017), national-level indicators of HAT elimination as a public health problem were defined (see section 7.4).

For the validation of g-HAT elimination, a template for national dossiers was developed. A first validation dossier submitted by Togo and a draft dossier submitted by Cameroon were used to assess the appropriateness of the template and to build the assessment criteria during the third HAT-e-TAG meeting in 2018. The surveillance plan for the post-validation phase (chapter 7 of the dossier) is especially important. Furthermore, the country validation dossier for g-HAT was adapted for r-HAT and a first version was submitted to this meeting for discussion (see section 7.2).
7.2 Country dossier for validation

The validation dossier documents the achievement of elimination of HAT as a public health problem by providing the information and requirements to demonstrate the absence of (or low level of) transmission. The key elements of the dossier are to assure the presence of a functional surveillance system capable of detecting possible cases. The version of the dossier adapted for r-HAT has eight chapters:

1. Description of the country and its capabilities
   1.1 General information about the country
       - Geographical, demographic, economic
       - Tourism activities in protected areas
   1.2 The country’s health system
       - Basic description, structures, capabilities
       - Utilization, attendance rates

2. Historical data and description of endemic areas
   2.1 Historical HAT data (essential)
       - Distribution of foci, control activities
       - Cases per year, at least since the 1960s
   2.2 Description/demarcation of current endemic areas (essential)
       - How the country defines endemic areas
       - Gray areas (potential, but no information)
       - Annual number of visitors

3. HAT surveillance and control activities
   3.1 Structure and capabilities to combat HAT (essential)
   3.2 Active screening strategy
   3.3 Passive screening strategy (essential)
   3.4 Response to suspected/confirmed cases (essential)
       - Concrete actions taken
   3.5 Analysis SWOT

4. HAT epidemiological data
   4.1 Current data, national level (essential)
   4.2 Data for the past 5 years, by health district (essential)
       - HAT cases (S1/S2), malaria testing (blood smear/RDT)
   4.3 Data following the national indicator of elimination (essential)
   4.4 HAT in neighbouring countries

5. Vector control
   5.1 Vector control strategy
       - Approach, protocols/tools and methods for evaluating results
       - Time-period, spatial coverage in relation to the presence of the disease
   5.2 Vector control linked to HAT, results
• Tsetse distribution maps, if possible by species
• Tsetse density data, tracked over time
• Proportion of flies infected with trypanosomes pathogenic for humans

6. Interventions regarding animals
6.1 Data on AAT
  • Farming systems, presence of *Trypanosoma brucei* in animals, livestock density
6.2 Capabilities to combat AAT
  • Actors, methods, coverage, links with the health sector
6.3 Activities for One Health
  • Animal intervention strategies for HAT control
  • Links with the health sector
  • Partners

7. Plan of post-validation surveillance (essential)
7.1 Elimination status must be monitored
  • Surveillance and response activities
7.2 Plan of surveillance for the next 5 years
  • Resources available, partners involved
7.3 To maintain the acquired status
7.4 Move towards the elimination of the transmission

8. References and annexes
The dossier allows health ministries to formally submit to WHO the claim of HAT elimination and the supporting data. A template is available in French and English. Eligible countries are encouraged to apply for validation and are invited also to provide constructive feedback so as to improve the process.

7.3 Validation process
An ad-hoc reviewing validation team will be constituted to evaluate the completeness, accuracy and reliability of a given country dossier. The team ascertains the likelihood that HAT is no longer a public health problem in the country, that the indicators established for this purpose are met, and that the surveillance system proposed is adequate and able to detect any re-emergence of the disease before reaching epidemic levels. The team of 1–2 experts is identified from a panel of experts selected by the WHO Regional Office for Africa plus 1–2 experts from HAT e-TAG and members of the WHO secretariat (WHO Regional Office for Africa and WHO Department of Control of Neglected Tropical Diseases). Following the template, each team member prepares a report that will be shared. The WHO secretariat coordinates the process and prepares the final report, which is agreed on. The final report is also submitted to the WHO Regional Office for review Africa and, if agreed, endorsed by the Regional Director. Finally, the WHO Director-General formally notifies the Ministry of Health in writing, and the information is published in the Weekly Epidemiological Record and the Global Health Observatory. A reassessment is foreseen after 5 years. Figure 7.3.1 shows the pathway for validation.
In the discussion, it was proposed that the experiences gained and the procedures established for validation be published to serve as an example of good practice for other diseases to follow on the path towards elimination.

### 7.4 National indicators – country status

The **global target** for elimination of HAT as a public health problem by 2020 is defined as follows:

- < 2000 cases reported annually at continental level
- 90% reduction of the total area at risk reporting ≥ 1 case/10 000 people per year (from 2004 baseline levels)

The global target and the indicators are not directly applicable at country level; they must be adapted in a simple and easily measurable way to the national context.

The **target at country level** for the elimination of HAT as a public health problem by 2020 was defined by HAT-e-TAG as follows:

- < 1 case/10 000 people in all health districts of the country during the previous five-year period

A health district is the internationally accepted health administrative and operational division (health measures implementation unit). This geographical area includes all components of a health system required to deliver community health care.

To calculate the national indicators, the numerator is the mean number of cases reported annually for the previous 5 years in a district. Cases are notified by the national sleeping sickness control programme in the health district according to the national case definition. The 5-year period smooths any variations of coverage and reporting from one year to another.
The denominator is the population of the health district at the mid-year period. The sources for estimating the health district population could vary (census, data collected by the national programme or by the health system, data from geospatial datasets, etc.) and therefore the source should be specified in the reporting.

The indicator is calculated for each health district. All districts of the country should have < 1 case/10 000 people, as an average of the previous 5 years. There is no overall calculation for the country. This indicator preserves the idea of the global indicator but greatly simplifies the calculation of the denominator for national programmes. However, health districts are not homogeneous, standardized entities. The indicator could thus be biased by the presence of population agglomerations in the district. The area of HAT transmission can also overlap several districts. Therefore, the assessment of the quality of the data provided and the local characteristics will be essential. Figure 7.4.1 categorizes the eligibility of countries in which r-HAT is endemic according to national indicators and control and surveillance activities to facilitate the request for validation of elimination.

**Figure 7.4.1.** Eligibility of r-HAT endemic countries for claiming validation of elimination, by epidemiological situation and status of surveillance and control activities, as of 2018

<table>
<thead>
<tr>
<th>Two criteria</th>
<th>Epidemiological situation (national indicator for elimination)</th>
<th>Activities of control and surveillance</th>
<th>Eligible for claiming the validation</th>
<th>Need to reinforce the surveillance before claiming the validation</th>
<th>Non eligible for the validation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 1 case/10 000 people per year, by health district, averaged over the previous 5-year period</td>
<td>True in all districts</td>
<td>Not true in one or more districts</td>
<td>Kenya, Rwanda</td>
<td>Malawi</td>
</tr>
</tbody>
</table>

Currently, one country (Togo) has requested validation of the elimination of g-HAT and three countries (Benin, Cameroon and Guinea) are preparing their country dossiers. Five countries are expected to be validated by 2020 (including one r-HAT endemic country) and 15 countries by 2025 (including 3–4 r-HAT endemic countries). Eligible countries are encouraged to apply for validation.

### 7.5 NTD roadmap 2030: targets and indicators

In 2012, WHO established the goal to eliminate HAT (g-HAT and r-HAT) as a public health problem by 2020. The global target is defined as:

- < 2000 cases reported annually at continental level
- 90% reduction of the total area at risk reporting ≥ 1 case/10 000 people per year (from 2004 baseline levels)
Beyond that, the goals for elimination of g-HAT and r-HAT by 2030 differ as follows:

- To interrupt transmission (sustainable elimination) of g-HAT by 2030
  - Indicator: cases of g-HAT declared per year
  - Target: zero cases by 2030
- To maintain elimination of r-HAT as a public health problem by 2030
  - Indicator: area endemic for r-HAT reporting ≥ 1 case/10,000 people per year
  - Target: no area endemic for r-HAT reporting ≥ 1 case/10,000 people per year by 2030

The reliability of the indicators is strongly dependent on the capacity to detect cases, and underreporting is a special concern for r-HAT.

When measuring progress towards elimination of r-HAT as a public health problem, milestones should be defined (e.g., 2023, 2025, 2027) and different indicators and targets considered, namely:

- **Number of r-HAT cases reported.** This indicator has been used until now. It is expected that the number of cases will decrease, but it is difficult to define a figure as a target and milestones. In 2030, the number of cases of r-HAT should be sporadic.

- **Areas of high or moderate risk (reporting ≥ 1 case/10,000 people per year).** These areas are expected to decrease to 0 in 2030 and milestones should be defined.

- A secondary indicator is required to indicate the expected improvement in **access to diagnosis and treatment for people at risk**, namely:
  - the at-risk population living within 1 hour’s travel of a competent facility (under discussion)
  - the at-risk population living within 5 hours’ travel of a competent facility (under discussion)
  - the proportion of HAT cases receiving appropriate treatment (> 99%)

- As a process indicator, a certain number of **countries should be validated progressively for elimination of HAT as a public health problem:**
  - In 2021: at least five countries
  - In 2025: at least 15 countries (3–4 r-HAT)

These targets are included in the framework of the new NTD roadmap (2021–2030). Goal 3.3 of the United Nations Sustainable Development Goals is, by 2030, “to end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases [including HAT] and combat hepatitis, water-borne diseases and other communicable diseases”. The global target for NTDs is, by 2030, to reduce by 90% the number of people requiring interventions against NTDs. During 2019, WHO will adopt indicators and targets for 2030 for all NTDs and publish them in 2020 as part of the new NTD roadmap.
8. Strategies for elimination of rhodesiense HAT

8.1 Overview of elimination efforts

The life-cycle of r-HAT is mostly zoonotic, involving both domestic and wild animals as the main reservoirs of the parasite and of the vector Glossina spp., commonly known as the tsetse fly. Occasionally, humans acquire the infection as accidental hosts, which although a relatively rare event provokes severe illness, deterioration and death unless cases are diagnosed and treated promptly. As the life-cycle of r-HAT involves many hosts, multiple interventions are available targeting different parts of the parasite life-cycle (Figure 8.1.1).

Figure 8.1.1. Life-cycle of r-HAT and methods of intervention targeting different stages of the disease

Numerous sectors are involved in r-HAT control beyond human health – such as veterinary services, vector control, tourism and management services of protected areas as well as wildlife – all of which contribute to a One Health approach. Each sector leads specific activities, which differ by country, but all sectors can and should actively collaborate in their respective fields in surveillance and IEC activities. Involvement from local authorities is also needed.

The methods used to control the vector include tsetse screens and traps, the sterilized insect technique (release of sterile tsetse males), insecticide impregnated net fencing and large-scale insecticide spraying (ground or aerial). Personal protection methods such as use of insect repellents and minimizing skin exposure are also promoted for populations that may be at risk.
Approaches to r-HAT control may vary based on the presence of wildlife reservoirs versus cattle reservoirs, for which different monitoring and control methods are required. Active screening is rarely applicable for areas in which wild animals are the main reservoir, but passive screening can be effective. Protected areas and parks are a vital source of income for countries and should be recognized as high priorities for surveillance by policy-makers. Incorporating this One Health approach is important ecologically and for local workers, who are constantly exposed.

For areas in which cattle are the main reservoir, active and passive screening is the method used. Treatment of cattle as a preventive or curative measure is seen to contribute significantly to the elimination of HAT and, additionally, protects cattle against other infections. Treatment includes spraying the legs and belly of cattle with insecticide (restricted application protocol).

Interventions on humans is the sector covered by WHO and include diagnosis of human cases (case-finding) and treatment. If a surveillance system is in place, WHO can produce pertinent information on disease distribution that helps to target interventions more effectively in all sectors. Data collected by the country and submitted to WHO are verified and entered into the Atlas of HAT, which is made available to countries and partners on request. It was noted that country-level risk assessments should take into consideration all components of epidemiological information, which could help towards achieving the goal of elimination and sustained surveillance. For example, countries should ensure that health-care facilities record the location of likely transmission, as this is more informative than the patient’s hometown. They should also ensure that exported cases are included in the country reports. This is especially important now that the intensity of transmission is reduced.

WHO offers training on diagnostics for clinical and laboratory staff, provides equipment and materials (including treatment) to national programmes and supports the supervision of health facilities offering HAT services (e.g. refreshing awareness periodically, providing advice when requested). Antitrypanosomal medicines are donated free of charge thanks to the partnership established with Sanofi and Bayer for the past 18 years. WHO is responsible for forecasting the amounts needed and where they need to be allocated, and provides guidance on how the supply should be used effectively and before expiry.

WHO is responsible also for advocating continued support from national authorities, international actors and the scientific community, especially as the incidence of the disease declines and thus has limited appeal and awareness to many. Raising awareness of the disease also applies to exposed populations and health-care workers.

While promoting the elimination of r-HAT is certainly within WHO’s remit, its scope of action is limited to the human health sector. The Organization’s strength lies in its convening power and ability to coordinate national and international actors, devise common strategies and plan activities. To eliminate the disease, interaction between national health workers and veterinary scientists must be stimulated, as they will be responsible for eliminating the disease from the animal reservoir. At the international level, WHO is collaborating with relevant organizations, namely FAO (the Food and Agriculture Organization of the United Nations), IAEA and OIE (the World Organisation for Animal Health). Consolidating this interaction will be crucial to achieving the elimination goal.

8.2 Strategies for elimination: case-finding

The most important decision for successful case-finding is the choice of surveillance sites. Site selection is the responsibility of the national programme coordinator. Surveillance sites need to be near areas of transmission and be well attended and sufficiently staffed (always consider existing facilities first), with laboratory facilities present and experienced staff and accessibility/communication with the central level. Countries have sent WHO an exhaustive list of health facilities that conduct clinical diagnosis, parasitological diagnosis and disease staging for r-HAT. This list will be updated regularly to track changes, as it is useful for management as well as for mapping the health coverage of endemic areas.
The distribution of health-care facilities layered over the distribution of r-HAT risk can inform countries about how to improve the positioning of facilities to cover a larger number of susceptible people (Figure 8.2.1). Areas with reported infections but no health-care facilities can indicate neglected areas, as distance from health-care facilities is a main contributing factor for health-seeking behaviour from patients. An extreme example can be seen in Zimbabwe, where the only HAT-competent diagnostic facility is located in Harare, hundreds of kilometers away from transmission areas.

Figure 8.2.1. Positioning of surveillance sites relative to risk areas (a) Malawi, (b) Uganda, (c) United Republic of Tanzania, (d) Rwanda, (e) Zambia, (f) Zimbabwe, (g) Kenya
Other ways of improving case-finding include training clinical staff to better recognize the signs and symptoms of r-HAT, with the use of support tools such as posters or information sheets. A checklist of frequent symptoms can aid clinical staff in diagnosing r-HAT and help to highlight its presence in endemic areas. Cascade training for peripheral health facilities is a way of building capacity and cost-effectively spreading knowledge of the disease outwards from sentinel sites. It is important to examine how health systems work in each country, as each country has its own needs. Decisions about diagnostic testing rely on the clinician, so awareness efforts and guidance should target clinicians. Improving awareness of r-HAT among traditional healers could also be beneficial for supporting early referral to health facilities.

Training laboratory staff can also improve case-finding. For example, each local network could be given a customized decision tree of available diagnostic methods, ranging from simple to complex, in addition to posters and information sheets on r-HAT. Often, diagnostics are unavailable due to a lack of equipment, which should be reviewed and reinforced by the national programme where needed. Microscopy slides of laboratory examinations should be saved for quality control and competency assessment, together with samples/images/videos of trypanosomes that can be used to refresh staff knowledge and be passed on to new staff. Regular supervision is needed for quality control and motivation of staff. It was noted that a supervisor’s checklist could be useful (already developed for g-HAT).

Active screening for r-HAT is usually reactive rather than prospective. It targets the family and village of the infected person and should be done immediately. Currently, active screening is based on parasitological screening of a selected population. Data collection on the number of suspected, tested and confirmed cases could help in monitoring trends in the incidence of the disease. A questionnaire has been introduced in some countries targeted at referring doctors, relating to the details of suspected cases (patient history, travel, activities).

### 8.3 Strategies for elimination: treatment

Treatment for r-HAT must be rapid and readily available. The medicines, available free of charge, must be ordered in time and the supplies must be appropriately managed by the national programmes. WHO provides guidance and technical support on managing supply and has also mapped health-care facilities which provide treatment, based on data submitted by countries. This information is all fed back to national focal points and summary data are available online.

### 8.4 Strategies for elimination: epidemiological surveillance

Surveillance of r-HAT starts with collection, validation and consolidation of data by the national coordinator, who prepares the reports for partners including WHO. These data are included in the global HAT Atlas by WHO in a process that involves checks for coherence and consistency. Any verification queries are sent to country coordinators in order to maximize data validity.

Emphasis is given to establishing and reporting the most probable place of infection of all HAT cases, as this information has important epidemiological value. All cases diagnosed in non-endemic countries (i.e. exported cases) are included and mapped at their most probable place of infection, and the national focal points are informed accordingly.

Surveillance data are essential for planning control and elimination of HAT. For example, the mapping of transmission areas by stratified levels of risk allows the best location of sentinel sites and identification of areas that are not well covered.

Countries have contributed significantly to the development and updating of the HAT Atlas and have expressed their interest in using the tool at country level. Countries have undergone training and been provided with equipment and software to use the Atlas for their benefit.
8.4 Strategies for elimination: IEC (information, education, communication)

The IEC strategy aims to increase awareness of r-HAT among: (i) exposed populations (i.e. on where to seek healthcare and what protective measures to use); (ii) health-care workers around sentinel sites, to remain aware of r-HAT as a possible diagnosis and provide information to patients being referred; (iii) traditional healers, as they are often the first people patients seek help from and must therefore be included in a positive way to encourage prompt referral of patients presenting HAT-compatible symptoms.

There is a potential role for the private sector in this strategy. Hotels and parks have a large stake in protecting their animals, their staff and their visitors, and have the resources to promote better awareness of r-HAT. If transmission areas include national parks, messaging should be retargeted to those areas that tourists may visit and hotel staff may frequent. As technology advances, anthropological surveys have demonstrated that the communication channels that people use currently are very different from past methods, e.g. mobile devices. Suggestions included a social media campaign on the dangers of r-HAT and protective measures, or training programmes on protective measures for hotel staff.

There is also a need to delineate between messaging regarding protection of livestock (which was a very successful campaign) and messaging regarding wildlife reservoirs because the populations at risk have very different demographics (local residents versus tourists, respectively). Tourists are more likely to travel to larger health-care facilities such as hospitals for early diagnosis, whereas local residents may have limited access to health care and so messaging should focus on them.

8.6 Strategies for elimination: coordination

The HAT elimination network coordinates the efforts of a wide range of stakeholders against HAT (Figure 8.6.1). Its role is to convene partners in order to identify gaps in control efforts and to develop common strategies for elimination. National coordination bodies are very important members of the network that evaluate progress and plan activities within the endemic countries.

Figure 8.6.1. The HAT elimination network

In the discussion, the importance of socio-anthropological aspects of r-HAT at the community level was recognized, including for the earlier detection of cases. It was recommended that this subject should be addressed.

South Africa is not endemic for r-HAT, but cases are regularly imported by medical evacuation flights from south and east African countries. With more than 60 patients treated for r-HAT in the past 18 years, important lessons about clinical management could be learnt. The experience was gathered in a high resource setting with intensive care management; however, it can be also adapted for less well-resourced areas. Most patients were treated in a private hospital in Johannesburg. A hospital pharmacy repository allows 24-hour access to medicines free of charge. Telephone consultancy or delivery of medicines for other medical facilities abroad is also provided.

More detailed data on the 20 treated cases were presented. Most patients were tourists; the others had an occupational-related exposure (Table 9.1). The patients acquired their infection in Malawi, Uganda, the United Republic of Tanzania, Zambia and Zimbabwe (Table 9.2).

Table 9.1. Reasons for exposure of imported r-HAT cases in South Africa, 2004–2014

<table>
<thead>
<tr>
<th>Reason</th>
<th>No. of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreign tourist</td>
<td>9</td>
</tr>
<tr>
<td>Expatriate or resident</td>
<td>4</td>
</tr>
<tr>
<td>Conservationist</td>
<td>2</td>
</tr>
<tr>
<td>Game farmer</td>
<td>2</td>
</tr>
<tr>
<td>Foreign soldier, field exercise</td>
<td>1</td>
</tr>
<tr>
<td>Pilot: tourist transport</td>
<td>1</td>
</tr>
<tr>
<td>Church-related travel</td>
<td>1</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>20</strong></td>
</tr>
</tbody>
</table>

Table 9.2. Country where the infection was acquired

<table>
<thead>
<tr>
<th>Country of acquisition</th>
<th>Number of cases and sites, 2004-2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malawi</td>
<td>6 (Kasungu 3, Nkhotakota 3)</td>
</tr>
<tr>
<td>Zambia</td>
<td>6 (Luangwa Valley 3, Kasanka 2, Kafue 1)</td>
</tr>
<tr>
<td>Tanzania</td>
<td>3 (Serengeti)</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>3 (Kariba 1, Mana Pools 2)</td>
</tr>
<tr>
<td>Uganda</td>
<td>2 (Queen Elizabeth National Park, Murcheson Falls)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>20</strong></td>
</tr>
</tbody>
</table>

The three key elements for the diagnosis were identified: (i) exposure in an endemic area; (ii) history of a painful tsetse bite; and (iii) presence of trypanosomal chancre. A trypanosomal chancre has a marked and painful erythema, but its appearance varies considerably (Figure 9.1). A chancre is not always present (< 50% of cases according to text books). Chancre is often missed, especially in parts of the body that are not obviously visible or are misinterpreted as insect bites or bacterial cellulites. A trypanosomal chancre is usually larger and has no obvious necrosis in contrast to an eschar in African tick bite fever.

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One of the biggest problems is a delayed diagnosis through poor history-taking, missing key clinical signs, delayed transfer, incorrect application of diagnostic tests and inexperienced laboratory personnel. In some endemic countries, local or expatriate doctors may not be aware of r-HAT, as it is a very rare disease. After the onset of symptoms, complications may develop in less than 1 week. Any extra delay may be critical and result in severe disease, with multorgan involvement, severe thrombocytopenia, frequent bleeding, renal failure, respiratory distress and hepatic pathology, requiring high levels of clinical care. **Myocarditis was only observed in an individual case.** Another rather early complication was fluid overload, which must be considered in intravenous fluid management. One case with complicated adrenal insufficiency was presented that has been described only once before. Decreased level of consciousness was in most cases not a sign of central nervous system (CNS) involvement and may have other explanations, such as metabolic derangements.

Initially, trypanosomes may be scanty and difficult to detect by microscopic examination of peripheral blood; therefore, blood smears should be repeated. Buffy coat films have an increased sensitivity, but they can be technically challenging to produce (e.g. centrifugation needed). Every patient, irrespective of clinical condition, must have an examination of cerebrospinal fluid (CSF). In South Africa, this is usually done after a few days of treatment with suramin, when the patient has clinically improved and the peripheral blood smear is clear of parasites. Otherwise, false-positive CSF findings from a “bloody tap” may be possible and there is a theoretical risk of introducing trypanosomes into CSF. The results of CSF should be interpreted not only in isolation but also in the clinical context; otherwise, they may lead to overdiagnosis of CNS involvement.

Treatment is usually started with a test dose of suramin. Adverse reactions including cardiovascular collapse, skin reactions, peripheral neuropathy and nephrotoxicity may occur. Only two patients were in the second stage and had to be treated with melarsoprol. Despite all the common problems described above, the mortality rate in the presented case series was low (2/20; 10%).

Successful case management relies on good laboratory facilities for rapid diagnosis, rapid access to antitrypanosomal treatment and skilled intensive care. Physicians in endemic countries are less and less experienced in the management of r-HAT. Besides operational research, recommendations should be developed that can be adapted to local conditions and especially for low resource settings.
10. Exported cases as surveillance tool for rhodesiense HAT

During 2000–2018, a total of 138 cases of HAT were reported from non-endemic countries (Figure 10.1).

**Figure 10.1. Numbers of cases of r-HAT diagnosed annually in non-endemic countries, 2000–2018**

Of these cases, 71% corresponded to the rhodesiense form and 29% to the gambiense form. Among the r-HAT cases, 82% were diagnosed in the first stage and 18% in the second stage. The vast majority of r-HAT cases were in tourists travelling to endemic areas (Table 10.1).

**Table 10.1. Cases of r-HAT diagnosed in nonendemic countries according to activity of the patient, 2000–2018**

<table>
<thead>
<tr>
<th>Activity</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tourists</td>
<td>74</td>
</tr>
<tr>
<td>Rangers</td>
<td>5</td>
</tr>
<tr>
<td>Tourism workers (guides pilots, lodges staff)</td>
<td>4</td>
</tr>
<tr>
<td>Conservationists workers</td>
<td>3</td>
</tr>
<tr>
<td>Soldiers</td>
<td>2</td>
</tr>
<tr>
<td>Hunters</td>
<td>1</td>
</tr>
<tr>
<td>Missionary</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>8</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>98</strong></td>
</tr>
</tbody>
</table>
HAT cases were diagnosed in nonendemic countries in the five continents. In South Africa, a frequent destination for medical evacuation flights from south and east African countries, the highest number (31 of r-HAT imported cases) was diagnosed, followed by the United States (20), the United Kingdom (12), the Netherlands (8), Belgium (4), Germany, India, Italy (3 each), China, Norway, Sweden (2 each) and Argentina, Brazil, Canada, France, Israel, Poland and Spain (1 each).

The infection was mainly contracted in protected areas such as national parks and wildlife reserves. The country exporting the most (47) r-HAT cases was the United Republic of Tanzania, mainly from the Serengeti National Park. For example, a cluster of cases that originated in the United Republic of Tanzania was suggestive of a change in the local epidemiology in 2001. The other countries exporting r-HAT cases were Zambia (20), Malawi (15), Zimbabwe (7), Uganda (7) and Kenya (2).

During 2000–2018, some 1.7% of all cases was reported from nonendemic countries (Table 10.2). The proportion of cases in whom r-HAT was diagnosed in nonendemic countries versus those diagnosed in endemic countries increased in the last years (2014–2018). The various factors for the increasing proportion of r-HAT cases diagnosed in non-DECs were discussed. Underreporting in endemic countries may be one factor. Better control of the domestic animal reservoir, in contrast to a lack of control of the wildlife reservoir in typical transmission zones for tourists, may be another factor.

Table 10.2. Cases of r-HAT by country of infection and proportion of cases diagnosed in nonendemic countries (exported cases) during 2000–2018 (left) and 2014–2018 (right)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Exported</td>
</tr>
<tr>
<td>Kenya</td>
<td>40</td>
<td>2</td>
</tr>
<tr>
<td>Malawi</td>
<td>695</td>
<td>15</td>
</tr>
<tr>
<td>Mozambique</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Tanzania</td>
<td>1,660</td>
<td>47</td>
</tr>
<tr>
<td>Uganda</td>
<td>3,281</td>
<td>7</td>
</tr>
<tr>
<td>Zambia</td>
<td>137</td>
<td>20</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>30</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>5,845</td>
<td>98</td>
</tr>
</tbody>
</table>

While the risk of infection is low for the total number of tourists, it cannot be disregarded. Awareness in health staff of travel medicine services of the risk of HAT is thus important.

As rapid access to antitypanosomal treatment is crucial for patients, WHO maintains strategic stocks in various non-endemic countries and an emergency stock in Geneva, Switzerland (Figure 10.2). Country-specific regulations for the import of medicines must be considered. Their distribution via the WHO country offices may be helpful to avoid delays.
Antitrypanosomal medicines are donated by Sanofi and Bayer and distributed solely under the responsibility of WHO. They cannot be obtained commercially (except for pentamidine, which is used to treat diseases other than HAT). The medicines are provided to countries in which the disease is endemic through WHO country offices, upon request, according to the needs and information provided. To treat HAT cases diagnosed in nonendemic countries, pharmaceutical services should request the medicines from WHO and provide epidemiological and clinical data on cases in whom the disease is diagnosed. This information enables WHO to maintain an HAT surveillance system for nonendemic countries that provides valuable information on “spots” of transmission to complement the data collected in endemic countries. This information is provided directly to the endemic countries and can be used to trigger specific activities.
11. Clinical trial for treatment of rhodesiense HAT with fexinidazole

Fexinidazole is the first effective oral monotherapy against both stages of g-HAT. It received a positive scientific opinion by the European Medicines Agency in November 2018, and marketing authorization was given in the Democratic Republic of the Congo in December 2018.

The clinical trial (FEX07) is due to start in May 2019 and will be conducted in Uganda and Malawi to assess the efficacy of fexinidazole for r-HAT patients.

Fexinidazole can be considered a prodrug that is metabolized into fexinidazole sulfoxide (M1) and fexinidazole sulfone (M2). The concentration of fexinidazole sulfone is decisive for the therapeutic effect. Fexinidazole must be taken with food. The plasma levels are highest if taken with high fat food, but high plasma levels are also reached with rice or plumpy-nut. The predicted CNS concentration levels, with 40% free fraction of fexinidazole sulfone, are clearly within therapeutic levels.

Safety data are available from the pooled analysis of the three main studies (FEX04, FEX05 and FEX06), including 619 patients with g-HAT. Gastrointestinal disorders, mainly vomiting and nausea, and CNS-related disorders (headache, insomnia, tremor) were the most commonly reported adverse events. The incidence of vomiting was higher in the paediatric study (FEX06) than in the adult study and was particularly high in the loading phase of the treatment (36% on day 2, the total schedule being 10 days). The majority of patients vomited more than 2 h after drug administration, likely triggered at CNS level. Importantly, however, with the exception of 2 patients, there were no severe events of vomiting and treatment could be continued.

The HAT-r-ACC consortium (ACC stands for access) was presented. Coordinated by DNDi with partners from France, Malawi, Portugal, Switzerland, and Uganda, its aims are: (i) to extend the indication of fexinidazole for the treatment of r-HAT (WP1); (ii) to ensure proper execution of the clinical trial through strengthened capacity for treatment and care (WP2); and (iii) to engage the local community to improve access to treatment and extend case detection (WP3). The project management Committee (WP4) includes representatives from DNDi, Institut de Recherche pour le Développement, the University of Lisbon, Makerere University of Uganda, Malawi Ministry of Health and Population, the Uganda National Health Research Organisation, the Swiss Tropical and Public Health Institute and Epicentre. It was emphasized that the trainings not only serve the trial but also enable community engagement through local staff. The programme is mainly funded by the European & Developing Countries Clinical Trials Partnership.
Protocol number: DNDI-FEX-07-HAT

Study title: Efficacy and safety of fexinidazole in patients with human African trypanosomiasis (HAT) due to Trypanosoma brucei rhodesiense: a multicentre, open-label clinical trial

Design: multicentre, open-label, non-randomized

Recruitment targets: 34 evaluable stage-2 r-HAT patients (stage-1 patients will be included but do not influence the statistical analyses)

Study sites: Lwala Hospital (Uganda) and Rumphi District Hospital (Malawi).

Patients from neighboring health centers: Kaberamaido/Dokolo districts (Uganda) and Rumphi/Mzimba North districts (Malawi) and Chama (Zambia) will be transported to the sites for treatment

Study duration: 2 years recruitment and 1-year follow-up

Main inclusion criteria
- Signed informed consent form
- ≥ 6 years old
- ≥ 20 kg body weight
- Ability to ingest at least one complete meal per day
- Karnofsky index ≥ 40
- Parasitological confirmation of T. b. rhodesiense infection
- Having a permanent address or being traceable by others and willing and able to comply with follow-up visit schedule
- Agreement to be hospitalized for a minimum of 11 days and to receive the study treatment

Main exclusion criteria
- Active clinically relevant medical conditions other than HAT that may jeopardize subject safety or at the investigator's discretion may interfere with participation in the study
- Compromised general health or severely deteriorated general condition, such as severe malnutrition, cardiovascular shock, respiratory distress or terminal illness
- Patients with severe hepatic impairment
- First trimester of pregnancy
- Any contraindication to nitroimidazole class (known hypersensitivity) or to any of the excipients
- Patients previously enrolled in the study or having already received fexinidazole

Treatment: fexinidazole 10 days (same regimen as in g-HAT), in 2 phases
- 2 doses depending on the patient's age and weight:
  - All adults and children (≤ 15 years old) ≥ 35kg:
    - D1 to D4 (1800 mg/day)
    - D5 to D10 (1200 mg/day)
  - Children weighing ≥ 20 and < 35 kg:
    - D1 to D4 (1200 mg/day)
    - D5 to D10 (600 mg/day)

Follow up visits: after 1 month, 9 weeks, 6 months and 12 months
Test of cure at 6 and 12 months including thick/thin blood smear and/or lymph node aspirate microscopic examination, lumbar puncture for parasite detection and CSF white blood cell count.
The initial data are expected for the beginning of 2021 and it is envisaged that the final results will be made available in the second quarter of 2023.

In the discussion, a regular update on progress of the study was proposed (e.g. at the next (fourth) stakeholders meeting). Some participants shared their optimism in reaching the recruitment target, as the clinical trial will raise awareness of the disease.

The potential of acoziborole, a single oral dose treatment, was also discussed. The clinical trial recruited 206 patients in stages 1 and 2 of g-HAT, most of them in late stage 2, and was completed in March 2019. In April 2014, about 30% of patients had completed the follow up period of 18 months. The absorption of acoziborole is less dependent on food than that of fexinidazole.
12. One Health: linking elimination of rhodesiense HAT with other initiatives

12.1 Epidemiological studies in animals and tsetse flies, and new molecular approaches in Zambia

Luapula province, in the north of Zambia, bordering the Democratic Republic of the Congo, was a historic focus of r-HAT, with no reported human cases since 2000. However, after 2 cases of r-HAT were reported (in 2017 and 2018), a biological survey was conducted in cattle at the location of the last case (in Samfya). Blood from 40 cattle was analysed with PCR (LAMP) for trypanosomes, yielding positive results for tsetse-transmitted animal trypanosomes, but not for human infective forms.

A study combining microscopy and molecular techniques determined the presence of trypanosome species in cattle, goats and tsetse flies in the Luangwa valley, north-eastern Zambia, but did not identify species infective to humans. Some further tsetse surveys in northern and central Zambia found samples positive for serum-resistance associated protein (SRA) (in varying proportions), indicative for T. b. rhodesiense, mainly in Glossina morsitans, the main vector for r-HAT (Figure 12.1.1). As these areas are currently considered at low, very low or no risk of transmission, the need for surveillance of HAT in these areas was suggested.

As the currently available tsetse traps are ineffective against G. morsitans, a new mobile, car mountable trap (“Sugimoto Trap”) was developed. The trap is easy to produce at low cost and minimizes exposure to flies during operation. The trap was tested in various national parks in Zambia and Malawi and found to be effective against G. morsitans, G. pallidipes and G. brevipalpes.

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To improve epidemiological knowledge of African trypanosomiasis, better tools are required to monitor trypanosome genotypes circulating in both mammalian hosts and tsetse fly vectors. Genotyping of trypanosome species is possible. A single test approach for accurate, sensitive detection and taxonomic characterization of trypanosomes by comprehensive analysis of internal transcribed spacer 1 amplicons was presented. Blood meal analysis of tsetse flies showed that flies can blood feed not only from common hosts such as warthog, kudu, buffalo, human, or cattle, but also from fruit-bats and rodents.

In the discussion, exchange with other groups (from FAO/IAEA division) working on mobile tsetse fly traps was encouraged. The importance of mapping the absence of *T. b. rhodesiense* was acknowledged.

### 12.2 Tsetse control and the management of r-HAT

There are different tsetse fly control strategies. For example, ground spraying is extensively used in Zimbabwe and aerial spraying in Botswana. In central and southern Uganda, cattle are insecticide treated with the restricted application protocol to control r-HAT (Stamping Out Sleeping Sickness campaign). However, many r-HAT foci in east and southern Africa are associated with wilderness areas, where this control method cannot be applied. Small insecticide-treated targets (“tiny targets”) are deployed over 4000 km² of northern Uganda (endemic areas for g-HAT) and suppressed the tsetse population by > 80% for more than 4 years. Tiny targets are not as cost-effective against savannah tsetse flies and hence this method is appropriate only in areas where *T. b. rhodesiense* is transmitted by *G. f. fuscipes*. Larger, traditional traps are used in Kenya, Malawi, the United Republic of Tanzania, Zambia and Zimbabwe. Table 12.1 shows the several competent vector species of HAT with their variable distributions across endemic countries.

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Table 12.1. Competent Glossina vectors of HAT and numbers of reported human cases by endemic country

<table>
<thead>
<tr>
<th>Country</th>
<th>Primary vectors</th>
<th>Other vectors</th>
<th>HAT cases 2000–2009</th>
<th>HAT cases 2010–2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uganda</td>
<td>G. f. fuscipes</td>
<td>Morsitans group</td>
<td>2848</td>
<td>431</td>
</tr>
<tr>
<td>Malawi</td>
<td>G. morsitans</td>
<td></td>
<td>471</td>
<td>209</td>
</tr>
<tr>
<td>Zambia</td>
<td>G. morsitans, G. pallidipes</td>
<td></td>
<td>82</td>
<td>50</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>G. morsitans, G. pallidipes</td>
<td></td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>United Republic of Tanzania</td>
<td>G. swynnertoni, G. pallidipes</td>
<td>Palpalis group</td>
<td>14</td>
<td>24</td>
</tr>
<tr>
<td>Kenya</td>
<td>G. swynnertoni, G. pallidipes</td>
<td>Palpalis group</td>
<td>38</td>
<td>2</td>
</tr>
</tbody>
</table>

Geostatistical models using remotely-sensed data have potential to identify sites of relatively high vector abundance, for surveillance and control, beyond the spatial extent of initial sampling.12

In a field investigation, tsetse and T. b. rhodesiense were unexpectedly scarce in an area outside the Serengeti National Park, where they were predicted to be abundant. An explanation was the frequent use of insecticide treatments against ticks and tsetse flies by livestock keepers. A simulation model has been developed showing the impact of insecticide-treated cattle depending on the frequency of use. Interventions by livestock keepers on cattle and the wider environment are reducing the abundance of tsetse in farming areas and thereby reducing the risk of r-HAT. A further simulation model has been developed that allows the impact of various control interventions to be predicted. Even a limited deployment of targets around the edge of Vwaza National Park (Malawi) was predicted to reduce the risk of HAT.

A simulation model has been developed to test whether recent increases in temperature in the Mana Pools National Park of the Zambezi Valley of Zimbabwe could account for the simultaneous decline of tsetse flies.13 The model suggests that the increase in temperature may explain the observed decrease of tsetse flies. It provides a first step in linking temperature to trypanosomiasis risk. Conversely, new disease foci may emerge with allocation of flies in higher, previously cooler regions.

A guidance document on tsetse fly control tools, specifying ideal measurements, colours, materials and deployment methods in different environments to make them fit for purpose is needed to enhance the implementation and efficacy of these tools. A working group of tsetse control practitioners across g-HAT and r-HAT endemic countries as well as WHO support for vector control recommendations was therefore requested.


Uganda: the last large-scale operation ended in 2012. A number of follow up proposals are not yet funded. Traps and targets, and cattle spraying are deployed in selected areas. Vector control activities are done by partners in selected HAT hotspots.

South Sudan: the political instability is hindering initiation of vector control activities.

United Republic of Tanzania: low level vector control activities (network of dip tanks) are undertaken; large scale operations are not funded. A national tsetse and trypanosomiasis control strategy is under development.

Kenya: the last large-scale operations concluded in 2012–2013. ICIPE is promoting repellent technology in selected areas. Kenya is apparently free of HAT (but this status is questionable in the Masai Mara–Serengeti ecosystem).

Rwanda: there are limited vector control activities in Akagera National Park. The last case of HAT was in 1998.

Burundi: there are virtually no vector control activities. The HAT status is not defined.

Zimbabwe: vector control activities are well advanced.

Zambia: vector control is progressing well with governmental commitment (e.g. aerial spraying).

Botswana and Namibia: both countries are applying for registration to be tsetse free.

The intensity of vector control activities varies greatly across regions. Large-scale vector control operations face challenges to funding. Governments should consider targeting vector control in areas of HAT transmission, also to assess the contribution of vector control to HAT elimination. Awareness/advocacy for vector control should be raised at the highest political level.

A PATTEC communication/advocacy strategy, prepared and supported by IAEA, targets political players at the highest level. There is increased engagement with Regional Economic Communities advocating for regional programmes. Recently, meetings have been held with the East African Community, the Economic Community of West African States and the Economic Community of Central African States.

Specialized Technical Committees and the Statutory Ministerial Forum on Agriculture, Rural Development, Water and Environment are platforms from which political awareness can be enhanced and recommendations then made to the Executive Council for decisions of African Heads of State and Government. Side events held during summits of the African Union on thematic issues, retreats with politicians on thematic issues, briefing sessions of the Permanent Representative Committee and with Ambassadors of Member States of the Committee of the African Union, which report to national capitals on the outcomes of briefing sessions, offer further possibilities to raise awareness.

A proposed way forward is collaboration among PATTEC, WHO and other partners on the preparation of policy briefs on HAT elimination. Summit decisions informed by policy briefs could commit African Heads of State and Government to the HAT elimination strategy.

In the discussion, the highly effective programmes in Ethiopia and Senegal were mentioned, which use the sterile insect technique for tsetse control. The PATTEC declaration of 2001 on the eradication of the tsetse fly is being reviewed, although limited staffing in the PATTEC coordination office makes this task challenging.
12.4 FAO and PATT: the progressive control pathway (PCP) for African animal trypanosomosis

The Programme Against African Trypanosomosis (PAAT) was officially established in November 1997 by the 29th Session of the FAO Conference (resolution 5/97). An interagency collaboration, PAAT coordinates the work of FAO, WHO, the IAEA and the Inter-African Bureau for Animal Resources of the African Union.

The vision of PAAT is an African continent where trypanosomoses no longer constrain sustainable agriculture and rural development, nor threaten human health. PAAT is funded by a regular budget from FAO, an annual contribution from WHO (for work on the HAT Atlas) and extrabudgetary contributions to FAO (including from the Government of Italy).

Partners of PAAT are AU-PATTEC, African Member States affected by tsetse and trypanosomiasis (38 sub-Saharan countries), OIE, the International Fund for Agricultural Development and the United Nations Industrial Development Organization. There are international cooperations for development and cooperations with civil society (Italian Cooperation, United Kingdom Department for International Development, Global Alliance for Livestock Veterinary Medicines). Partnering research institutes are based in Africa (Centre International de Recherche-Développement sur l'Elevage en Zone Subhumide, CIPE, International Livestock Research Institute, National Agriculture Research Systems and academia) as well as in Europe (IRD/CIRAD [Cooperation Internationale en Recherche Agronomique pour le Développement], ITM). Health for Animals (formerly the International Federation for Animal Health) is a private-sector partner.

FAO promotes the progressive control pathway (PCP) for AAT as a strategic framework to reduce the disease burden. It also promotes One Health interventions (e.g. livestock protective fences). The Atlases of tsetse and AAT (i.e. continental and national) have been developed, and WHO is supported in the Atlas of HAT. Capacity development and technical support for endemic countries is provided, as well as knowledge products (e.g. publications, web site, news, seminars, support to research, etc.).

While great strides have been made in the elimination of HAT, progress in the control of AAT lags behind. PCPs are used for the control of a number of human and animal diseases, e.g. *peste de petits ruminents*, brucellosis and rables. International organizations such as FAO, WHO, OIE and AU rely on PCP frameworks to plan, implement and evaluate interventions. The operational development of a PCP for AAT was led by FAO (in the framework of PAAT), in collaboration with IAEA, AU-PATTEC and CIRAD, and in consultation with OIE and WHO. PCP is a stepwise approach of five stages plus a pre-entry (“below stage 1”) level (Figure 12.4.1). Progression from one stage to another is possible only if the set goals are met and the following stage is prepared. An independent validation of stage progression is required.

At the pre-entry level, political commitment and a functioning specialized national structure with core capacities that is mandated to deal with tsetse and AAT are essential requirements for entering PCP. In stage 1, affected countries develop technical capacities and gain sufficient understanding of AAT distribution, risk and impact for evidence-based planning of subsequent activities. Pilot field interventions are also conducted. Larger scale field activities are implemented in stage 2 and beyond. Stage 2 aims to achieve sustainable, economically-profitable reductions in AAT burden. The intervention strategy is based on integrated management of AAT (a community/farmer-based approach). The aim of the final stages (3–5) of PCP is to create sustainable AAT-free areas. Stage 3 is completed when AAT transmission is interrupted. In stage 4, some control measures are maintained, while in stage 5 the elimination of AAT must be sustainable in the absence of interventions.

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During the 17th AU-PATTEC Coordinators’ Meeting (26–28 November 2018) it was recommended that the PCP concept be streamlined into national and regional strategies and projects against AAT. Stakeholders have been engaged in three AU-PATTEC meetings as well as in several workshops in AAT-affected countries in eastern Africa since 2015.

AAT is an OIE notifiable disease. There is no official recognition by OIE of “freedom from AAT”; however, country self-declarations of freedom are possible. The first AAT-specific chapter in the OIE Terrestrial Code will provide an opportunity to close a gap for AAT. FAO supports this effort and participates in meetings with a view to ensuring consistency with PCP.

In the discussion, the possibility of Member States applying for funding of small-scale technical projects via the FAO country representative was raised.
13. Conclusions

The participants of the third stakeholders meeting concluded as follows.

1. The low number of reported r-HAT cases indicates that the goal of elimination of HAT as a public health problem by 2020 is within reach. Nevertheless, under-detection remains a concern and surveillance should be reinforced in response. WHO maintains its commitment to supporting countries endemic for the disease in ensuring access to diagnosis and treatment for r-HAT patients and in monitoring the epidemiological progression of the disease.

2. Wildlife and domestic animals constitute the main reservoirs of r-HAT and play a central role in maintaining transmission to humans through the bite of infectious tsetse flies. In this epidemiological context, vector control should be strengthened and animal health interventions deployed in a One Health framework to attain r-HAT elimination. The use of the progressive control pathway approach for African animal trypanosomiasis could be useful in promoting synergies for control of the animal reservoir and the vector.

3. Given the variability in the characteristics and quality of vector control tools, guidelines should be prepared to ensure the quality and good use of vector control tools tailored to different environments.

4. New tools for r-HAT diagnosis and surveillance that can be adapted for use in the field should be developed as a priority.

5. The widespread use of rapid diagnostic tests for malaria has reduced the use of blood smear microscopy and thereby diminished the probability of diagnosing r-HAT. Therefore, in areas endemic for r-HAT, clinical and laboratory algorithms including blood smear microscopy should be designed and applied for diagnosis of r-HAT.

6. Progress has been made in the possible introduction of new treatments for r-HAT. Fexinidazole has been approved for treatment of gambiense-HAT and a clinical trial is expected to start shortly. Updates on this trial should be presented at the next (fourth) stakeholders meeting. A new stage-independent single dose oral treatment with acoziborole could offer other possibilities for treatment.

7. Advances in the process of validation of elimination of r-HAT as a public health problem have been made, and eligible countries are encouraged to apply for validation. WHO should make publicly available the material it has developed, including templates for country dossiers, as well as the procedures and criteria for assessing them. This material could also be used to raise awareness of HAT and could represent a blueprint for other diseases targeted for elimination to follow.

8. The significant funding gap in control, research and awareness-raising activities calls for advocacy by external donors; national appropriation including domestic financing is critical also for sustainable r-HAT elimination.

9. The gaps in diagnostic, treatment and vector control capacities, mainly in terms of trained staff, together with the loss of expertise and frequent rotation of skilled personnel, are worrisome and should be addressed. Possible solutions include engaging health authorities subnationally and optimizing expert resources nationally and internationally, including in cascade training.

10. Aid materials and manuals for improvement of patient management in endemic areas and of exported cases should be prepared.

11. r-HAT activities should be integrated into other health programmes as a means of reinforcing control and surveillance of r-HAT.

12. The important socio-anthropological aspects of r-HAT at the community level, including the potential facilitation of earlier detection of cases and access to treatment, should be addressed alongside surveillance and control activities.

13. r-HAT stakeholders are encouraged to engaged in the ongoing process of developing indicators, targets and milestones for the new NTD roadmap 2021–2030.
## Annex 1. Agenda

### Day 1 – Wednesday 10 April 2019: Description of the situation of HAT and progress

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Presenter/Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:00–09:30</td>
<td>Welcome</td>
<td>WHO AFRO Representative Director, WHO/CDS/NTD</td>
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<tr>
<td>09:30–09:45</td>
<td>Introduction to the meeting</td>
<td>Coordinator, WHO/CDS/IDM Chairperson</td>
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<tr>
<td>10:00–11:00</td>
<td>Global situation of r-HAT</td>
<td>WHO</td>
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<td>14:00–16:00</td>
<td>Elimination of rhodesiense HAT as a public health problem in 2020</td>
<td>V. Lejon</td>
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<td>14:00–16:00</td>
<td>HAT elimination Technical Advisory Group (HAT-e-TAG): specific r-HAT aspects</td>
<td>WHO</td>
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<td>16:00–17:00</td>
<td>Strategies for elimination. Reinforced integrated surveillance:</td>
<td>WHO</td>
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<td></td>
<td>– Selection of sites</td>
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<td>– Capacity-building in diagnosis and treatment</td>
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<td>– Management of drugs</td>
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<td>– Monitoring and evaluation</td>
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<td>– Reporting</td>
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<td>NTD roadmap 2030: target 2030 (indicators and targets)</td>
<td>WHO</td>
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### Day 2 – Thursday 11 April 2019: Control and elimination of r-HAT

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Presenter/Notes</th>
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<tbody>
<tr>
<td>09:00–09:30</td>
<td>Clinical management of complicated cases of HAT Case management protocols</td>
<td>L. Blumberg</td>
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<tr>
<td>09:30–10:00</td>
<td>Exported cases as a surveillance tool for HAT</td>
<td>WHO</td>
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<td>10:30–12:30</td>
<td>Clinical trial for treatment of r-HAT with fexinidazole</td>
<td>N Strub, A Tarral, O. Valverde</td>
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<td>13:30–15:00</td>
<td>Contribution of other sectors to r-HAT elimination (One Health): linking elimination of r-HAT with other initiatives:</td>
<td>FAO/PATTEC/COCTU Open floor</td>
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<td>– Vector control</td>
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<td>– Animal health</td>
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<td>– Management of protected areas</td>
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<tr>
<td>15:00–16:00</td>
<td>Gaps and challenges</td>
<td>General discussion</td>
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<tr>
<td>16:00–17:00</td>
<td>Conclusions, outcomes and closure of meeting</td>
<td>General discussion</td>
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</table>
Annex 2. List of participants

Members

Professor M. Barrett,1 University of Glasgow, Glasgow, Scotland, United Kingdom
Dr J. Bernard, Ministry of Health, Community Development, Gender, Elderly and Children, Dodoma, United Republic of Tanzania
Dr S. Biéler, Foundation for Innovative New Diagnostics, Geneva, Switzerland
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Dr R. Grais,1 Epicentre, Paris, France
Mr R. Argiles Herrero,1 International Atomic Energy Agency, Vienna, Austria
Dr G. Hesse,1 Bayer Environmental Science, Ecully, France
Mrs R. Kasati,1 Ministry of Health, Nairobi, Kenya
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Dr A. Lidner, Institute of Tropical Medicine and International Health, Berlin, Germany
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Professor S. Torr, Liverpool School of Tropical Medicine, Liverpool, United Kingdom
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Dr C. Wamboga, Ministry of Health, Kampala, Uganda
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Dr G. Priotto, Innovative & Intensified Disease Management, Department of Control of Neglected Tropical Diseases, World Health Organization, Geneva, Switzerland
Dr P.P. Simarro, Consultant, Geneva, Switzerland

Report of the third WHO stakeholders meeting on rhodesiense human African trypanosomiasis
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Geneva, Switzerland, 10–11 April 2019